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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS  4  MAY 10   CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  5  MAY 11   KOREAPAT updates resume
 NEWS  6  MAY 19   Derwent World Patents Index to be reloaded and enhanced
 NEWS  7  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  8  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS  9  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 10  JUN 26   TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 11  JUN 28   Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 12  JUl 11   CHEMSAFE reloaded and enhanced
 NEWS 13  JUl 14   FSTA enhanced with Japanese patents
 NEWS 14  JUl 19   Coverage of Research Disclosure reinstated in DWPI
 NEWS 15  AUG 09   INSPEC enhanced with 1898-1968 archive
 NEWS 16  AUG 28   ADISCTI Reloaded and Enhanced
 NEWS 17  AUG 30   CA(SM)/CAplus(SM) Austrian patent law changes
 NEWS 18  SEP 11   CA/CAplus enhanced with more pre-1907 records
 NEWS 19  SEP 21   CA/CAplus fields enhanced with simultaneous left and right
                   truncation
 NEWS 20  SEP 25   CA(SM)/CAplus(SM) display of CA Lexicon enhanced
 NEWS 21  SEP 25   CAS REGISTRY(SM) no longer includes Concord 3D coordinates
 NEWS 22  SEP 25   CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
 NEWS 23  SEP 28   CEABA-VTB classification code fields reloaded with new
                   classification scheme

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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FILE 'HOME' ENTERED AT 00:59:31 ON 02 OCT 2006

=> file uspatful
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 28 Sep 2006 (20060928/PD)
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HIGHEST APPLICATION PUBLICATION NUMBER: US2006218687
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REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006

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=> e dwyer john/in
E1            3     DWYER JEFF/IN
E2            6     DWYER JENNIFER SUE/IN
E3            6 --> DWYER JOHN/IN
E4            1     DWYER JOHN A/IN
E5            1     DWYER JOHN E/IN
E6            1     DWYER JOHN EDWARD JR/IN
E7           18     DWYER JOHN J/IN
E8            1     DWYER JOHN JAMES/IN
E9            1     DWYER JOHN MICHAEL/IN
E10           1     DWYER JOHN R/IN
E11           1     DWYER JOHN ROBERT/IN
E12           1     DWYER JOSEPH G/IN

=> s e3-e11
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              1 "DWYER JOHN E"/IN
              1 "DWYER JOHN EDWARD JR"/IN
             18 "DWYER JOHN J"/IN
              1 "DWYER JOHN JAMES"/IN
              1 "DWYER JOHN MICHAEL"/IN
              1 "DWYER JOHN R"/IN
              1 "DWYER JOHN ROBERT"/IN
L1           31 ("DWYER JOHN"/IN OR "DWYER JOHN A"/IN OR "DWYER JOHN E"/IN OR
                "DWYER JOHN EDWARD JR"/IN OR "DWYER JOHN J"/IN OR "DWYER JOHN
               JAMES"/IN OR "DWYER JOHN MICHAEL"/IN OR "DWYER JOHN R"/IN OR
               "DWYER JOHN ROBERT"/IN)

=> s l1 and (HR1 or HR2)
            521 HR1
            432 HR2
L2            2 L1 AND (HR1 OR HR2)

=> d l2,cbib,clm,1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L2   ANSWER 1 OF 2  USPATFULL on STN
2004:120446 Method for production of antivirals by use of HIV-derived HR1
    peptides, and trimers formed therefrom.
    Dwyer, John, Chapel Hill, NC, UNITED STATES
    Delmedico, Mary K., Raleigh, NC, UNITED STATES
    US 2004091855 A1 20040513
    APPLICATION: US 2003-671316  A1  20030924 (10)
    PRIORITY: US 2002-414515P  20020927 (60)
    DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM    What is claimed is:
       1. A method for identifying a compound that inhibits transmission of HIV
       to a target cell, the method comprising contacting synthetic peptide
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comprising trimers in the presence of a compound and with HR2 peptide under conditions and for a time sufficient to allow formation of a complex between the synthetic peptide comprising trimers and HR2 peptide in vitro; and detecting the amount of complex formed; wherein inhibition or reduction of complex formation in the presence of the compound, as compared to complex formation in the absence of the compound, is indicative of ability of the compound to inhibit transmission of HIV to a target cell; and wherein synthetic peptide comprises an amino acid sequence derived from the HR1 region of HIV-1 gp41; wherein the HR1 region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the HR1 region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the HR1 region, which enables synthetic peptide to self-assemble in solution into trimers.

2. The method according to claim 1, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising either a substitution in the "c" position, or a substitution in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

3. The method according to claim 2, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

4. The method according to claim 1, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" that are in a position of the heptad repeat positions selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

5. The method according to claim 4, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the "a" position, a "d" position, a "b" position, and a combination thereof.

6. The method according to claim 1, wherein the synthetic peptide further comprises a component selected from the group consisting of one or more reactive functionalities, a macromolecular carrier, a pharmaceutically acceptable carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

7. The method according to claim 1, wherein the synthetic peptide is

predominately in trimeric form.

8. The method according to claim 1, wherein the synthetic peptide is in a monomer-trimer equilibrium.

9. A method for producing a drug that inhibits transmission of HIV to a target cell, the method comprising contacting synthetic peptide comprising trimers in the presence of a compound and with **HR2** peptide under conditions and for a time sufficient to allow formation of a complex between the synthetic peptide comprising trimers and **HR2** peptide in vitro; and detecting the amount of complex formed; wherein inhibition or reduction of complex formation in the presence of the compound is indicative of ability of the compound to inhibit transmission of HIV to a target cell; and wherein the drug comprises the compound contacted with a pharmaceutically acceptable carrier in producing the drug; and wherein synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the **HR1** region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.

10. The method according to claim 9, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising either a substitution in the "c" position, or a substitution in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

11. The method according to claim 10, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

12. The method according to claim 9, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" that are in a position of the heptad repeat positions selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

13. The method according to claim 12, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the "a" position, a "d" position, a "b" position, and a combination thereof.

14. The method according to claim 9, wherein the synthetic peptide further comprising a component selected from the group consisting of one

or more reactive functionalities, a macromolecular carrier, a pharmaceutically acceptable carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

15. The method according to claim 9, wherein the synthetic peptide is predominately in trimeric form.

16. The method according to claim 9, wherein the synthetic peptide is in a monomer-trimer equilibrium.

17. In a method for identifying or producing a molecule that can inhibit the binding between **HR1** and **HR2** regions of HIV gp41, the improvement which comprises: use of a trimer as a binding partner with **HR2** peptide in detecting in vitro the ability of the molecule to bind to an HR (heptad repeat) region of HIV gp41; wherein the trimer is comprised of synthetic peptide comprising an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the **HR1** region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.

18. The method according to claim 17, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising either a substitution in the "c" position, or a substitution in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

19. The method according to claim 18, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

20. The method according to claim 17, wherein the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" that are in a position of the heptad repeat positions selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

21. The method according to claim 20, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the "a" position, a "d" position, a "b" position, and a combination thereof.

22. The method according to claim 17, wherein the synthetic peptide further comprising a component selected from the group consisting of one or more reactive functionalities, a macromolecular carrier, a pharmaceutically acceptable carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

L2 ANSWER 2 OF 2 USPATFULL on STN
2004:100776 HIV-derived **HR1** peptides modified to form stable trimers, and their use in therapy to inhibit transmission of human immunodeficiency virus.
Delmedico, Mary Kay, Raleigh, NC, UNITED STATES
Dwyer, John, Chapel Hill, NC, UNITED STATES
US 2004076637 A1 20040422
APPLICATION: US 2003-664021 A1 20030916 (10)
PRIORITY: US 2002-414514P 20020927 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:
1. A synthetic peptide comprising an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the **HR1** region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.

2. The synthetic peptide according to claim 1, wherein the one or more amino acid substitutions in the hydrophobic domain comprise either a substitution in the "c" position, or a substitution in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

3. The synthetic peptide according to claim 2, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

4. The synthetic peptide according to claim 1, wherein the one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" are in a position of the heptad repeat positions selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

5. The synthetic peptide according to claim 4, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group

consisting of the "a" position, a "d" position, a "b" position, and a combination thereof.

6. The synthetic peptide according to claim 1, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

7. The synthetic peptide according to claim 2, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

8. The synthetic peptide according to claim 3, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

9. The synthetic peptide according to claim 4, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

10. The synthetic peptide according to claim 5, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

11. A trimer formed from synthetic peptide according to claim 1.

12. The trimer according to claim 11, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

13. A trimer formed from synthetic peptide according to claim 2.

14. The trimer according to claim 13, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

15. A trimer formed from synthetic peptide according to claim 3.

16. The trimer according to claim 15, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

17. A trimer formed from synthetic peptide according to claim 4.

18. The trimer according to claim 17, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

19. A trimer formed from synthetic peptide according to claim 5.

20. The trimer according to claim 19, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

21. A synthetic peptide comprising an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the amino acid sequence comprises a heptad repeat containing a plurality of heptads, and a hydrophobic domain comprising heptad repeat positions "efgabcdef" corresponding to amino acids 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the synthetic peptide comprises an amino acid substitution in either the "c" position of the hydrophobic domain, or in both the "g" position and the "c" position of the hydrophobic domain, as compared to native sequence of the **HR1** region; wherein the amino acid substitution enables the synthetic peptide to self-associate in solution into trimers.

22. The synthetic peptide according to claim 21, wherein the synthetic peptide comprises an amino acid substitution, as compared to native sequence of the **HR1** region, additional to a substitution in a "c" position or in both the "g" position and "c" position; wherein the additional amino acid substitution is in one or more heptads of the synthetic peptide; and wherein the additional amino acid substitution is in one or more amino acid positions selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

23. The synthetic peptide according to claim 21, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

24. The synthetic peptide according to claim 22, further comprising a

component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

25. A trimer formed from synthetic peptide according to claim 21.

26. The trimer according to claim 25, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

27. A trimer formed from synthetic peptide according to claim 22.

28. The trimer according to claim 27, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

29. A synthetic peptide comprising an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the amino acid sequence comprises a heptad repeat containing a plurality of heptads, and a hydrophobic domain comprising heptad repeat positions "efgabcdef" corresponding to amino acids 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the synthetic peptide comprises an amino acid substitution in one or more of an "e" position at the C-terminus of the hydrophobic domain, an "f" position at the C-terminus of the hydrophobic domain, or a combination thereof, as compared to native sequence of the **HR1** region; and wherein the amino acid substitution enables the synthetic peptide to self-associate in solution into trimers.

30. The synthetic peptide according to claim 29, wherein the synthetic peptide comprises an amino acid substitution, as compared to native sequence of the **HR1** region, additional to the substitution in one or more of an "e" position and "f" position; wherein the additional amino acid substitution is in one or more heptads of the synthetic peptide; and wherein the additional amino acid substitution is in one or more amino acid positions selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

31. The synthetic peptide according to claim 29, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

32. The synthetic peptide according to claim 30, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide,

and a combination thereof.

33. A trimer formed from synthetic peptide according to claim 29.

34. The trimer according to claim 33, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

35. A trimer formed from synthetic peptide according to claim 30.

36. The trimer according to claim 35, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

37. A synthetic peptide comprising an amino acid sequence selected from the group of amino acid sequences consisting of: SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:43, SEQ ID NO:81, and SEQ ID NO:82.

38. The synthetic peptide according to claim 37, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

39. A trimer formed from synthetic peptide according to claim 37.

40. The trimer according to claim 39, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

41. A trimer formed from self-association of synthetic peptide in solution, wherein the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the **HR1** region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; wherein the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and wherein the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-associate in solution into trimers.

42. The trimer according to claim 39, further comprising a component

selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

43. A trimer formed from self-association of synthetic peptide in solution, wherein the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the amino acid sequence comprises a heptad repeat containing a plurality of heptads, and a hydrophobic domain comprising heptad repeat positions "efgabcdef" corresponding to amino acids 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the synthetic peptide comprises an amino acid substitution in either the "c" position of the hydrophobic domain, or in both the "g" position and the "c" position of the hydrophobic domain, as compared to native sequence of the **HR1** region; and wherein the amino acid substitution enables the synthetic peptide to self-associate in solution into trimers.

44. The trimer according to claim 43, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

45. A trimer formed from self-association of synthetic peptide in solution, wherein the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the amino acid sequence comprises a heptad repeat containing a plurality of heptads, and a hydrophobic domain comprising heptad repeat positions "efgabcdef" corresponding to amino acids 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the synthetic peptide comprises an amino acid substitution in either the "c" position of the hydrophobic domain or in both the "g" position and the "c" position of the hydrophobic domain, as compared to native sequence of the **HR1** region; wherein the synthetic peptide also comprises an amino acid substitution, additional to the substitution in the "c" position or in both the "g" position and "c" position, in one or more heptads of the synthetic peptide; wherein the additional amino acid substitution is in one or more amino acid positions selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof; and wherein the amino acid substitutions enable the synthetic peptide to self-associate in solution into trimers.

46. The trimer according to claim 45, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

47. A trimer formed from self-association of synthetic peptide in solution, wherein the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the amino acid sequence comprises a heptad repeat containing a plurality of heptads, and a hydrophobic domain comprising heptad repeat positions "efgabcdef" corresponding to amino acids 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the synthetic peptide comprises an amino acid

substitution in one or more of an "e" position at the C-terminus of the hydrophobic domain, an "f" position at the C-terminus of the hydrophobic domain, or a combination thereof, as compared to native sequence of the **HR1** region; and wherein the amino acid substitution enables the synthetic peptide to self-associate in solution into trimers.

48. The trimer according to claim 47, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

49. A trimer formed from self-association of synthetic peptide in solution, wherein the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; wherein the amino acid sequence comprises a heptad repeat containing a plurality of heptads, and a hydrophobic domain comprising heptad repeat positions "efgabcdef" corresponding to amino acids 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; wherein the synthetic peptide comprises an amino acid substitution in one or more of an "e" position at the C-terminus of the hydrophobic domain, an "f" position at the C-terminus of the hydrophobic domain, or a combination thereof, as compared to the native sequence of the **HR1** region; wherein the synthetic peptide also comprises an amino acid substitution, additional to the substitution in either or both of the "e" position and the "f" position, in one or more heptads of the synthetic peptide; wherein the additional amino acid substitution is in one or more amino acid positions selected from the group consisting of an "a" position, a "d" position, a "b" position", and a combination thereof; and wherein the amino acid substitutions enable the synthetic peptide to self-associate in solution into trimers.

50. The trimer according to claim 49, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

51. A trimer formed from self association of synthetic peptide in solution, wherein the synthetic peptide comprises an amino acid sequence selected from the group of amino acid sequences consisting of: SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:43, SEQ ID NO:81, and SEQ ID NO:82.

52. The trimer according to claim 49, further comprising a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimer, and a combination thereof.

53. A method for inhibition of transmission of HIV-1 to a cell comprising contacting the virus, in the presence of a target cell, with synthetic peptide in a concentration effective to inhibit infection of the cell by HIV-1, thereby inhibiting transmission of HIV-1 to the cell, wherein: the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; the **HR1** region consists of

native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids comprising the sequence corresponding to amino acid residues 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.

54. The method according to claim 53, wherein the one or more amino acid substitutions in the hydrophobic domain comprise a substitution in either the "c" position or in both the "g" position and the "c" position of the heptad repeat positions "efgabcdef".

55. The method according to claim 54, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in either the "c" position or in both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

56. The method according to claim 53, wherein the one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" are selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

57. The method according to claim 56, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

58. The method according to claim 53, wherein synthetic peptide further comprises a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

59. The method according to claim 53, wherein synthetic peptide is in an oligomeric form comprising trimers.

60. The method according to claim 59, wherein the trimers further comprise a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimers, and a combination thereof.

61. The method of claim 53, wherein the synthetic peptide is parenterally administered to an individual.

62. A method for inhibition of transmission of HIV-1 to a target cell comprising adding synthetic peptide to the virus and a target cell in an amount effective to inhibit infection of the cell by HIV-1, wherein: the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; the **HR1** region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids comprising the sequence corresponding to amino acid residues 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.

63. The method according to claim 62, wherein the one or more amino acid substitutions in the hydrophobic domain comprise a substitution in either the "c" position, or in both the "g" position and the "c" position, of the heptad repeat positions "efgabcdef".

64. The method according to claim 63, wherein the synthetic peptide comprises an amino acid substitution additional to a substitution in either the "c" position or both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

65. The method according to claim 62, wherein the one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" are selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

66. The method according to claim 65, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

67. The method according to claim 62, wherein synthetic peptide further comprises a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

68. The method according to claim 62, wherein synthetic peptide is in an oligomeric form comprising trimers.

69. The method according to claim 68, wherein the trimers further comprise a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino

acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimers, and a combination thereof.

70. The method of claim 62, wherein synthetic peptide is parenterally administered to an individual.

71. A method for inhibiting HIV fusion with a target cell comprising contacting the virus, in the presence of a target cell, with synthetic peptide in a concentration effective to inhibit membrane fusion between the virus and the cell, wherein: the synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; the **HR1** region consists of native amino acid sequence shown as SEQ ID NO:1 or polymorphisms thereof; the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids comprising the sequence corresponding to amino acid residues 28 to 36 of SEQ ID NO:1 or polymorphisms thereof; amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions "efgabcdef"; and the amino acid sequence of the synthetic peptide comprises one or more amino acid substitutions in the heptad repeat positions "efgabcdef" comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.

72. The method according to claim 71, wherein the one or more amino acid substitutions in the hydrophobic domain comprise a substitution in either the "c" position or in both the "g" position and the "c" position of the heptad repeat positions "efgabcdef".

73. The method according to claim 72, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in the "c" position or in both the "g" position and "c" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of the "a" position, a "d" position, a "b" position, and a combination thereof.

74. The method according to claim 71, wherein the one or more amino acid substitutions in the hydrophobic domain comprising the heptad repeat positions "efgabcdef" are selected from the group consisting of a C-terminal "e" position, a C-terminal "f" position, and a combination thereof.

75. The method according to claim 74, wherein the synthetic peptide comprises an amino acid substitution additional to the substitution in one or more of the "e" position and the "f" position, wherein the additional amino acid substitution is in one or more amino acid positions of one or more heptads of the synthetic peptide, and wherein the one or more amino acid positions is selected from the group consisting of an "a" position, a "d" position, a "b" position, and a combination thereof.

76. The method according to claim 71, wherein synthetic peptide further comprises a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of the synthetic peptide, and a combination thereof.

77. The method according to claim 71, wherein synthetic peptide is in an oligomeric form comprising trimers.

78. The method according to claim 77, wherein the trimers further comprise a component selected from the group consisting of one or more reactive functionalities, a pharmaceutically acceptable carrier, a macromolecular carrier, an amino acid substitution comprising an addition of no less than one amino acid and no more than twenty amino acids to either or both of the amino terminus or carboxy terminus of synthetic peptide forming the trimers, and a combination thereof.

79. The method of claim 71, wherein synthetic peptide is parenterally administered to an individual.

```
=> e delmedico mary k/in
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E2            3     DELME ROGER ROBERT/IN
E3            2 --> DELMEDICO MARY K/IN
E4            1     DELMEDICO MARY KAY/IN
E5            1     DELMEDICO SUSAN G/IN
E6            2     DELMEE PETRUS H M/IN
E7            2     DELMEGE ARTHUR H/IN
E8            2     DELMEGE DALE/IN
E9            2     DELMEGE JAMES W/IN
E10           1     DELMENDO JON G/IN
E11           1     DELMENICO ANDREAS/IN
E12           1     DELMENICO JACK/IN

=> s e3-e4
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=> s l3 not l2
L4            1 L3 NOT L2

=> d l4,cbib

L4   ANSWER 1 OF 1  USPATFULL on STN
2003:253453 Methods and compositions for inhibition of membrane
    fusion-associated events including RSV transmission.
    Antczak, James B., Durham, NC, United States
    Delmedico, Mary K., Raleigh, NC, United States
    Erickson, Joel B., Durham, NC, United States
    Lambert, Dennis M., Durham, NC, United States
    Sista, Prakash, Durham, NC, United States
    Trimeris, Inc., Durham, NC, United States (U.S. corporation)
    US 6623741 B1 20030923
    APPLICATION: US 2000-515965  20000229 (9)
    DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> d l4,cbib,clm

L4   ANSWER 1 OF 1  USPATFULL on STN
2003:253453 Methods and compositions for inhibition of membrane
    fusion-associated events including RSV transmission.
    Antczak, James B., Durham, NC, United States
    Delmedico, Mary K., Raleigh, NC, United States
    Erickson, Joel B., Durham, NC, United States
    Lambert, Dennis M., Durham, NC, United States
```

Sista, Prakash, Durham, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)
US 6623741 B1 20030923
APPLICATION: US 2000-515965 20000229 (9)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
CLM What is claimed is:

1. An isolated peptide having a formula selected from the group consisting of: X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYI-Z; X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYID-Z; X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDK-Z; X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z; X-SKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z; X-AVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z; X-AVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQL-Z; and X-SGVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQL-Z (SEQ ID NOS: 1549, 1548, 1545, 1544, 1546, 1551, 1547, and 1550, respectively), in which amino acid residues are presented by the single-letter code; X comprises an amino group, an acetyl group, a 9-fluorenylmethoxy-carbonyl group, a hydrophobic group, or a macromolecular carrier group; Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

2. The isolated peptide of claim 1, wherein said peptide has the formula X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYI-Z (SEQ ID NO:1549).

3. The isolated peptide of claim 1, wherein said peptide has the formula X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYID-Z (SEQ ID NO:1548).

4. The isolated peptide of claim 1, wherein said peptide has the formula X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDK-Z (SEQ ID NO:1545).

5. The isolated peptide of claim 1, wherein said peptide has the formula X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z (SEQ ID NO:1544).

6. The isolated peptide of claim 1, wherein said peptide has the formula X-SKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z (SEQ ID NO:1546).

7. The isolated peptide of claim 1, wherein said peptide has the formula X-AVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z (SEQ ID NO:1551).

8. The isolated peptide of claim 1, wherein said peptide has the formula X-AVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQL-Z (SEQ ID NO:1547).

9. The isolated peptide of claim 1, wherein said peptide has the formula X-SGVAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQL-Z (SEQ ID NO:1550).

10. The isolated peptide of claim 1, wherein X comprises an amino group, an acetyl group, a 9-fluorenylmethoxy-carbonyl group, a hydrophobic group or a macromolecular carrier group; further wherein Z is an amido group.

11. The isolated peptide of claim 1, wherein Z comprises a carboxyl group, an amido group, a hydrophobic group or a macromolecular carrier group; further wherein X is an acetyl group.

12. The isolated peptide of claim 1, wherein X is an acetyl group, and Z is an amido group.

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=> file wpids
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    11.29      11.50

FILE 'WPIDS' ENTERED AT 01:01:25 ON 02 OCT 2006
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http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

=> e dwyer j/in
E1            2     DWYER HALLQUIST P/IN
E2            1     DWYER I N/IN
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              2 "DWYER J L"/IN
              2 "DWYER J M"/IN
              7 "DWYER J P"/IN
L5           58 ("DWYER J"/IN OR "DWYER J A"/IN OR "DWYER J C"/IN OR "DWYER J
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               "DWYER J L"/IN OR "DWYER J M"/IN OR "DWYER J P"/IN)

=> e e12
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E2            2     DWYER J M/IN
E3            7 --> DWYER J P/IN
E4            1     DWYER J P J/IN
```

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E6            3     DWYER J S/IN
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E9            1     DWYER JJ/IN
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=> s e1-e8
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             2 "DWYER J R"/IN
             3 "DWYER J S"/IN
             1 "DWYER J T"/IN
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              OR "DWYER J W"/IN)

=> s l5 or l6
L7          74 L5 OR L6

=> s l7 and (HR1 or HR2)
           162 HR1
           151 HR2
L8           2 L7 AND (HR1 OR HR2)

=> d l8,bib,ab,1-2

L8   ANSWER 1 OF 2  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2004-374930 [35]   WPIDS
DNC  C2004-140955
TI   Identifying compound inhibiting HIV transmission to target cell, comprises
     contacting synthetic peptide in presence of compound with heptad repeat
     peptide to form complex and identifying compound based on inhibition of
     complex formation.
DC   B04 D16
IN   DELMEDICO, M K; DWYER, J
PA   (DELM-I) DELMEDICO M K; (DWYE-I) DWYER J
CYC  1
PI   US 2004091855 A1 20040513 (200435)*      35
ADT  US 2004091855 A1 Provisional US 2002-414515P 20020927, US 2003-671316
     20030924
PRAI US 2002-414515P      20020927; US 2003-671316       20030924
AB   US2004091855 A UPAB: 20040603
     NOVELTY - Identifying (M1) compound that inhibits transmission of HIV to
     target cell, comprising contacting synthetic peptide (I) in presence of
     compound and with heptad repeat (HR2) peptide for forming complex
     between (I) and HR2 peptide, and detecting amount of complex formed,
     where inhibition or reduction of complex formation in presence of
     compound, indicates inhibition of HIV to target cell, is new.
          DETAILED DESCRIPTION - Identifying (M1) a compound that inhibits
     transmission of HIV to a target cell, comprises contacting a synthetic
     peptide (I) comprising trimers in the presence of a compound and with
     heptad repeat (HR2) peptide under conditions and for a time sufficient
     to allow formation of a complex between (I) comprising trimers and HR2
     peptide in vitro, and detecting the amount of complex formed, where
     inhibition or reduction of complex formation in the presence of the
```

compound, as compared to complex formation in the absence of the compound, is indicative of ability of the compound to inhibit transmission of HIV to a target cell.

INDEPENDENT CLAIMS are also included for:

(1) producing (M2) a drug that inhibits transmission of HIV to a target cell, comprising carrying out the contacting and detecting steps of (M1), where inhibition or reduction of complex formation in the presence of compound is indicative of ability of the compound to inhibit transmission of HIV to a target cell, and the drug comprises the compound contacted with the carrier in producing the drug; and

(2) identifying or producing (M3) a molecule that inhibits the binding between **HR1** and **HR2** regions of HIV gp41, where the improvement involves use of a trimer as a binding partner with **HR2** peptide in detecting in vitro the ability of the molecule to bind to an HR region of HIV gp41, where the trimer is comprised of (I).

ACTIVITY - Anti-HIV. No biological data given.

MECHANISM OF ACTION - Inhibitor of transmission of HIV to target cell (claimed); Inhibitor of interaction between **HR1** and **HR2** regions of HIV gp41; Vaccine.

In vitro analysis of molecules inhibiting binding interaction between **HR1** and **HR2** regions, was carried out as follows: About 20 micro l of solution containing desired concentration of molecule having ability to bind to trimers and either inhibit or disrupt **HR1-HR2** binding interactions, were added. Reference standards, e.g. predetermined amounts of known inhibitor of **HR1-HR2** binding interactions or no inhibitor, were added to other reaction wells not containing the molecule. To each reaction well 10 micro l of trimers formed from the synthetic peptide was added. After a sufficient time for the trimers to contact the molecule, 10 micro l of desired concentration of labeled **HR2** peptide was added to the reaction wells. The result indicated inhibition of binding interaction between **HR1** and **HR2** regions by the molecule. The molecule was then subjected to in vitro infectivity assay against HIV-1. The IC50 of the molecule was found to be 0.002 micro g/ml.

USE - (M1) is useful for identifying a compound that inhibits transmission of HIV to a target cell (claimed). The synthetic peptide of (M1) is useful for producing antiviral agents having activity against HIV. The compound identified by (M1) is useful as an antiviral agent for HIV.

DESCRIPTION OF DRAWING(S) - The figure is a graph representing use of synthetic peptide and heptad repeat (**HR2**) peptide for producing molecule that inhibits binding between **HR1** and **HR2** sequences.

Dwg.5/5

L8 ANSWER 2 OF 2 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-316084 [29] WPIDS
DNC C2004-119901
TI New synthetic peptide comprising an amino acid sequence derived from the **HR1** region of HIV-1 gp41, useful for inhibiting transmission of HIV-1 to a cell.
DC B04 D16
IN DELMEDICO, M K; **DWYER, J**
PA (DELM-I) DELMEDICO M K; (DWYE-I) DWYER J; (TRIM-N) TRIMERIS INC
CYC 102
PI WO 2004029074 A2 20040408 (200429)* EN 94
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
US 2004076637 A1 20040422 (200429)

AU 2003287011 A1 20040419 (200462)
AU 2003287011 A8 20051103 (200629)
ADT WO 2004029074 A2 WO 2003-US30286 20030926; US 2004076637 A1 Provisional US 2002-414514P 20020927, US 2003-664021 20030916; AU 2003287011 A1 AU 2003-287011 20030926; AU 2003287011 A8 AU 2003-287011 20030926
FDT AU 2003287011 A1 Based on WO 2004029074; AU 2003287011 A8 Based on WO 2004029074
PRAI US 2003-664021 20030916; US 2002-414514P 20020927
AB WO2004029074 A UPAB: 20040505
NOVELTY - A new synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41.
DETAILED DESCRIPTION - A new synthetic peptide comprises an amino acid sequence derived from the **HR1** region of HIV-1 gp41; where the **HR1** region consists of native 59-amino acid sequence or polymorphisms; where the **HR1** region from which the synthetic peptide is derived comprises a hydrophobic domain of amino acids corresponding to amino acid residues in positions 28 to 36 of 59-amino acid sequence or its polymorphisms; where the amino acid residues comprising the hydrophobic domain correspond to heptad repeat positions efgabcdef; and where the amino acid sequence of the synthetic peptide further comprises one or more amino acid substitutions in the heptad repeat positions efgabcdef comprising the hydrophobic domain, as compared to the native amino acid sequence of the **HR1** region, which enables synthetic peptide to self-assemble in solution into trimers.
INDEPENDENT CLAIMS are also included for the following:
(1) a trimer formed from synthetic peptide;
(2) a method for inhibiting transmission of HIV-1 to a cell;
(3) a method for inhibiting transmission of HIV-1 to a target cell; and
(4) a method for inhibiting HIV fusion with a target cell.
ACTIVITY - Anti-HIV. No biological data given.
MECHANISM OF ACTION - Gene therapy.
USE - The synthetic peptide is useful for inhibiting transmission of HIV-1 to a cell (claimed).
Dwg.0/4

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.06	23.56

FILE 'MEDLINE' ENTERED AT 01:02:10 ON 02 OCT 2006

FILE LAST UPDATED: 30 Sep 2006 (20060930/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> e dwyer j/au
E1            2     DWYER HARRY A/AU
E2            2     DWYER I M/AU
E3          153 --> DWYER J/AU
E4            1     DWYER J A/AU
E5            2     DWYER J C/AU
E6            6     DWYER J D/AU
E7            6     DWYER J E/AU
E8            3     DWYER J F/AU
E9            6     DWYER J G/AU
E10          47     DWYER J H/AU
E11           1     DWYER J H 3RD/AU
E12          19     DWYER J J/AU

=> s e3-e12
            153 "DWYER J"/AU
              1 "DWYER J A"/AU
              2 "DWYER J C"/AU
              6 "DWYER J D"/AU
              6 "DWYER J E"/AU
              3 "DWYER J F"/AU
              6 "DWYER J G"/AU
             47 "DWYER J H"/AU
              1 "DWYER J H 3RD"/AU
             19 "DWYER J J"/AU
L9          244 ("DWYER J"/AU OR "DWYER J A"/AU OR "DWYER J C"/AU OR "DWYER J
                D"/AU OR "DWYER J E"/AU OR "DWYER J F"/AU OR "DWYER J G"/AU OR
                "DWYER J H"/AU OR "DWYER J H 3RD"/AU OR "DWYER J J"/AU)

=> e e12
E1           47     DWYER J H/AU
E2            1     DWYER J H 3RD/AU
E3           19 --> DWYER J J/AU
E4            1     DWYER J JR/AU
E5            4     DWYER J L/AU
E6          118     DWYER J M/AU
E7            2     DWYER J N/AU
E8            4     DWYER J P/AU
E9            1     DWYER J R/AU
E10           5     DWYER J S/AU
E11           2     DWYER J S M/AU
E12         126     DWYER J T/AU

=> s e1-e12
             47 "DWYER J H"/AU
              1 "DWYER J H 3RD"/AU
             19 "DWYER J J"/AU
              1 "DWYER J JR"/AU
              4 "DWYER J L"/AU
            118 "DWYER J M"/AU
              2 "DWYER J N"/AU
              4 "DWYER J P"/AU
              1 "DWYER J R"/AU
              5 "DWYER J S"/AU
              2 "DWYER J S M"/AU
            126 "DWYER J T"/AU
L10         330 ("DWYER J H"/AU OR "DWYER J H 3RD"/AU OR "DWYER J J"/AU OR "DWYE
                R J JR"/AU OR "DWYER J L"/AU OR "DWYER J M"/AU OR "DWYER J N"/AU
                OR "DWYER J P"/AU OR "DWYER J R"/AU OR "DWYER J S"/AU OR "DWYER
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              J S M"/AU OR "DWYER J T"/AU)

=> e e12
E1            5     DWYER J S/AU
E2            2     DWYER J S M/AU
E3          126 --> DWYER J T/AU
E4           22     DWYER J W/AU
E5            1     DWYER J X/AU
E6            7     DWYER JAMES/AU
E7            8     DWYER JAMES H/AU
E8            1     DWYER JAMES T/AU
E9            1     DWYER JAMES W/AU
E10          10     DWYER JAMI/AU
E11           2     DWYER JAMI M/AU
E12           1     DWYER JAMIE P/AU

=> s e1-e12
              5 "DWYER J S"/AU
              2 "DWYER J S M"/AU
            126 "DWYER J T"/AU
             22 "DWYER J W"/AU
              1 "DWYER J X"/AU
              7 "DWYER JAMES"/AU
              8 "DWYER JAMES H"/AU
              1 "DWYER JAMES T"/AU
              1 "DWYER JAMES W"/AU
             10 "DWYER JAMI"/AU
              2 "DWYER JAMI M"/AU
              1 "DWYER JAMIE P"/AU
L11         186 ("DWYER J S"/AU OR "DWYER J S M"/AU OR "DWYER J T"/AU OR "DWYER
                J W"/AU OR "DWYER J X"/AU OR "DWYER JAMES"/AU OR "DWYER JAMES
                H"/AU OR "DWYER JAMES T"/AU OR "DWYER JAMES W"/AU OR "DWYER JAMI"
                /AU OR "DWYER JAMI M"/AU OR "DWYER JAMIE P"/AU)

=> e e12
E1           10     DWYER JAMI/AU
E2            2     DWYER JAMI M/AU
E3            1 --> DWYER JAMIE P/AU
E4            2     DWYER JASON R/AU
E5            2     DWYER JEANNE L/AU
E6            1     DWYER JEFF/AU
E7            1     DWYER JEFFREY W/AU
E8            1     DWYER JEREMY P/AU
E9            1     DWYER JOANNA/AU
E10          25     DWYER JOHANNA/AU
E11          25     DWYER JOHANNA T/AU
E12           5     DWYER JOHN/AU

=> d his

     (FILE 'HOME' ENTERED AT 00:59:31 ON 02 OCT 2006)

     FILE 'USPATFULL' ENTERED AT 00:59:40 ON 02 OCT 2006
               E DWYER JOHN/IN
L1            31 S E3-E11
L2             2 S L1 AND (HR1 OR HR2)
               E DELMEDICO MARY K/IN
L3             3 S E3-E4
L4             1 S L3 NOT L2

     FILE 'WPIDS' ENTERED AT 01:01:25 ON 02 OCT 2006
               E DWYER J/IN
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L5            58 S E3-E12
                 E E12
L6            28 S E1-E8
L7            74 S L5 OR L6
L8             2 S L7 AND (HR1 OR HR2)

     FILE 'MEDLINE' ENTERED AT 01:02:10 ON 02 OCT 2006
                 E DWYER J/AU
L9           244 S E3-E12
                 E E12
L10          330 S E1-E12
                 E E12
L11          186 S E1-E12
                 E E12

=> del l9-l11
DELETE L9-L11? (Y)/N:y

=> e dwyer john/au
E1            25      DWYER JOHANNA/AU
E2            25      DWYER JOHANNA T/AU
E3             5 --> DWYER JOHN/AU
E4             1      DWYER JOHN J/AU
E5            12      DWYER JOHN J M/AU
E6             4      DWYER JOHN M/AU
E7             2      DWYER JONATHAN/AU
E8             2      DWYER JOSEPH R/AU
E9             1      DWYER JOYCE CAROL/AU
E10            2      DWYER JOYCE L/AU
E11            1      DWYER JOYCE LISA E A/AU
E12            4      DWYER JOYCE P/AU

=> s e3-e6
              5 "DWYER JOHN"/AU
              1 "DWYER JOHN J"/AU
             12 "DWYER JOHN J M"/AU
              4 "DWYER JOHN M"/AU
L9           22 ("DWYER JOHN"/AU OR "DWYER JOHN J"/AU OR "DWYER JOHN J M"/AU OR
                "DWYER JOHN M"/AU)

=> s l9 and (HR1 or HR2)
            250 HR1
            202 HR2
L10           1 L9 AND (HR1 OR HR2)

=> d l10,cbib,ab

L10  ANSWER 1 OF 1     MEDLINE on STN
2003199173.     PubMed ID: 12718536.  The hydrophobic pocket contributes to the
     structural stability of the N-terminal coiled coil of HIV gp41 but is not
     required for six-helix bundle formation. Dwyer John J; Hasan Aisha;
     Wilson Karen L; White Jonathan M; Matthews Thomas J; Delmedico Mary K.
     (Trimeris, Inc., 3518 Westgate Drive, Durham, North Carolina 27707, USA. )
     Biochemistry, (2003 May 6) Vol. 42, No. 17, pp. 4945-53.  Journal code:
     0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.
AB   In models of HIV fusion, the glycoprotein gp41 is thought to form a
     six-helix bundle during viral fusion with the target cell.  This bundle is
     comprised of three helical regions (from the heptad repeat 2, or HR2,
     region of gp41) bound to an inner, trimeric, coiled-coil core (from the
     HR1 region).  Although much has been learned about the structure and
     thermodynamics of this complex, the energetics of the isolated HR1
     self-associated oligomer remain largely unknown.  By systematically
```

studying self-association through a series of truncations based on a 51-mer **HR1** peptide (T865), we have identified amino acid segments which contribute significantly to the stability of the oligomeric **HR1** complex. Biophysical characterization of C-terminal truncations of T865 identifies a 10-15-amino acid region that is essential for **HR1** oligomerization. This region coincides with a hydrophobic pocket that provides important contacts for the interaction of **HR2** helices. Complete removal of this pocket abolishes **HR1** oligomerization. Despite the dramatic reduction in stability, the monomeric **HR1** peptides are still able to form stable six-helix bundles in the presence of **HR2** peptides. Truncations on the N-terminal side of T865 have little effect on oligomerization but significantly reduce the stability of the **HR1-HR2** six-helix bundle. Unlike the **HR2** binding site, which extends along a hydrophobic groove on the **HR1** oligomer, the residues that are critical for **HR1** oligomerization are concentrated in a 10-15-amino acid region. These results demonstrate that there are localizations of binding energy, or "hot spots", in the self-association of peptides derived from the **HR1** region of gp41.

```
=> e delmedico m k/au
E1            1     DELMEDICO ANTONIETTA/AU
E2            1     DELMEDICO J/AU
E3            1 --> DELMEDICO M K/AU
E4            1     DELMEDICO MARY K/AU
E5            1     DELMEDICO P/AU
E6            1     DELMEDICO V J/AU
E7            1     DELMEE EVELYNE/AU
E8            1     DELMEE J/AU
E9           87     DELMEE M/AU
E10          15     DELMEE MICHEL/AU
E11           1     DELMEEE M/AU
E12           2     DELMEIRE D/AU

=> s e3 or e4
              1 "DELMEDICO M K"/AU
              1 "DELMEDICO MARY K"/AU
L11           2 "DELMEDICO M K"/AU OR "DELMEDICO MARY K"/AU

=> s l11 not l10
L12           1 L11 NOT L10

=> d l12,cbib,ab

L12  ANSWER 1 OF 1     MEDLINE on STN
2001031173.    PubMed ID: 11038187.   Evidence that the transition of HIV-1
     gp41 into a six-helix bundle, not the bundle configuration, induces
     membrane fusion. Melikyan G B; Markosyan R M; Hemmati H; Delmedico M K;
     Lambert D M; Cohen F S. (Department of Molecular Biophysics and
     Physiology, Rush Medical College, Chicago, Illinois 60612, USA. ) The
     Journal of cell biology, (2000 Oct 16) Vol. 151, No. 2, pp. 413-23.
     Journal code: 0375356. ISSN: 0021-9525. Pub. country: United States.
     Language: English.
AB   Many viral fusion proteins exhibit a six-helix bundle as a core structure.
     HIV Env-induced fusion was studied to resolve whether membrane merger was
     due to the transition into the bundle configuration or occurred after
     bundle formation. Suboptimal temperature was used to arrest fusion at an
     intermediate stage. When bundle formation was prevented by adding
     inhibitory peptides at this stage, membranes did not merge upon raising
     temperature. Inversely, when membrane merger was prevented by
     incorporating lysophosphatidylcholine (LPC) into cell membranes at the
     intermediate, the bundle did not form upon optimizing temperature. In the
```

absence of LPC, the six-helix bundle did not form when the temperature of the intermediate was raised for times too short to promote fusion. Kinetic measures showed that after the temperature pulse, cells had not advanced further toward fusion. The latter results indicate that bundle formation is the rate-limiting step between the arrested intermediate and fusion. Electrical measures showed that the HIV Env-induced pore is initially large and grows rapidly. It is proposed that bundle formation and fusion are each contingent on the other and that movement of Env during its transition into the six-helix bundle directly induces the lipid rearrangements of membrane fusion. Because peptide inhibition showed that, at the intermediate stage, the heptad repeats of gp41 have become stably exposed; creation of the intermediate could be of importance in drug and/or vaccine development.

```
=> file uspatful
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      1.61      25.17

FILE 'USPATFULL' ENTERED AT 01:04:00 ON 02 OCT 2006
CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 28 Sep 2006 (20060928/PD)
FILE LAST UPDATED: 28 Sep 2006 (20060928/ED)
HIGHEST GRANTED PATENT NUMBER: US7114185
HIGHEST APPLICATION PUBLICATION NUMBER: US2006218687
CA INDEXING IS CURRENT THROUGH 28 Sep 2006 (20060928/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 28 Sep 2006 (20060928/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2006
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2006


=> s (HIV or human immunodeficiency virus)
         45383 HIV
        522505 HUMAN
         25660 IMMUNODEFICIENCY
        105701 VIRUS
         18282 HUMAN IMMUNODEFICIENCY VIRUS
                  (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)
L13      47774 (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)

=> s l13 and (HR1 and HR2)
           521 HR1
           432 HR2
L14         64 L13 AND (HR1 AND HR2)

=> s l14 and (HR1/clm or HR2/clm)
            31 HR1/CLM
            25 HR2/CLM
L15          7 L14 AND (HR1/CLM OR HR2/CLM)

=> s l15 and ay<2003
       3800280 AY<2003
L16          0 L15 AND AY<2003

=> s l14 and ay<2003
       3800280 AY<2003
L17         26 L14 AND AY<2003

=> d l17,cbib,1-26
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L17 ANSWER 1 OF 26 USPATFULL on STN
2005:82251 Hbm variants that modulate bone mass and lipid levels.
Allen, Kristina, Hopkinton, MA, UNITED STATES
Anisowicz, Anthony, West Newton, MA, UNITED STATES
Graham, James R., Arlington, MA, UNITED STATES
Morales, Arturo, Arlington, MA, UNITED STATES
Yaworsky, Paul J., Rockland, MA, UNITED STATES
Liu, Wei, Sudbury, MA, UNITED STATES
US 2005070699 A1 20050331
APPLICATION: US 2004-477173 A1 20041104 (10)
WO 2002-US14877 20020513
PRIORITY: US 2001-290071P 20010511 (60)
US 2001-291311P 20010517 (60)
US 2002-353058P 20020201 (60)
US 2002-361293P 20020304 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 2 OF 26 USPATFULL on STN
2004:282022 Transgenic animal model of bone mass modulation.
Babij, Philip, Newbury Park, CA, UNITED STATES
Bex, Frederick James, Newton Square, PA, UNITED STATES
Bodine, Peter Van Nest, Havertown, PA, UNITED STATES
Askew, G. Roger, Boxford, MA, UNITED STATES
US 2004221326 A1 20041104
APPLICATION: US 2004-477238 A1 20040412 (10)
WO 2002-US14876 20020513
PRIORITY: US 2001-60290071 20010511
US 2001-60291311 20010517
US 2002-60353058 20020201
US 2002-60361293 20020304
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 3 OF 26 USPATFULL on STN
2004:211474 High bone mass gene of 1.1q13.3.
Carulli, John P., Southboro, MA, United States
Little, Randall D., Newtonville, MA, United States
Recker, Robert R., Omaha, NE, United States
Johnson, Mark L., Omaha, NE, United States
Genome Therapeutics Corporation, Waltham, MA, United States (U.S. corporation)
US 6780609 B1 20040824
APPLICATION: US 2000-543771 20000405 (9)
PRIORITY: US 1998-105511P 19981023 (60)
US 1998-71449P 19980113 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 4 OF 26 USPATFULL on STN
2004:192608 High bone mass gene of 11q13.3.
Carulli, John P., Southboro, MA, United States
Little, Randall D., Newtonville, MA, United States
Recker, Robert R., Omaha, NE, United States
Johnson, Mark L., Omaha, NE, United States
Genome Therapeutics Corporation, Waltham, MA, United States (U.S. corporation)Creighton University School of Medicine, Omaha, NE, United States (U.S. corporation)
US 6770461 B1 20040803
APPLICATION: US 2000-544398 20000405 (9)
PRIORITY: US 1998-105511P 19981023 (60)
US 1998-71449P 19980113 (60)

DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 5 OF 26 USPATFULL on STN
2004:146900 Methods and compositions for inhibition of membrane fusion-associated events, including **HIV** transmission.
Jeffs, Peter, Chapel Hill, NC, United States
Lackey, John William, Hillsborough, NC, United States
Erickson, Joel Burton, Durham, NC, United States
Lawless, Mary Katherine, Raleigh, NC, United States
Merutka, Gene, Saratoga, CA, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)
US 6750008 B1 20040615
APPLICATION: US 1999-350841 19990709 (9)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 6 OF 26 USPATFULL on STN
2004:133299 DIRECT MULTIPLEX CHARACTERIZATION OF GENOMIC DNA.
Willis, Thomas D., San Francisco, CA, UNITED STATES
Hardenbol, Paul, Los Altos, CA, UNITED STATES
Jain, Maneesh, Menlo Park, CA, UNITED STATES
Stolc, Viktor, Cupertino, CA, UNITED STATES
Ronaghi, Mostafa, Palo Alto, CA, UNITED STATES
Davis, Ronald W., Palo Alto, CA, UNITED STATES
US 2004101835 A1 20040527
APPLICATION: US 2001-999362 A1 20011024 (9)
PRIORITY: US 2000-242901P 20001024 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 7 OF 26 USPATFULL on STN
2004:88267 Immunogenic compositions comprising liver stage malarial antigens.
Cohen, Joe, Rixensart, BELGIUM
Druilhe, Pierre, Paris, FRANCE
US 2004067236 A1 20040408
APPLICATION: US 2003-415253 A1 20031024 (10)
WO 2001-EP12349 20011023
PRIORITY: EP 2000-203724 20001025
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 8 OF 26 USPATFULL on STN
2003:314633 Hybrid polypeptides with enhanced pharmacokinetic properties.
Barney, Shawn, Apex, NC, United States
Guthrie, Kelly I., Virginia Beach, VA, United States
Merutka, Gene, Saratoga, CA, United States
Anwer, Mohmed K., Foster City, CA, United States
Lambert, Dennis M., Cary, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)
US 6656906 B1 20031202
APPLICATION: US 1999-350641 19990709 (9)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 9 OF 26 USPATFULL on STN
2003:265218 Methods and compositions for synthesis of nucleic acid molecules using multiple recognition sites.
Chesnut, Jonathan D., Carlsbad, CA, UNITED STATES
Carrino, John, San Diego, CA, UNITED STATES
Leong, Louis, Mission Viejo, CA, UNITED STATES
Madden, Knut, Carlsbad, CA, UNITED STATES

Gleeson, Martin, San Diego, CA, UNITED STATES
Fan, James, Carlsbad, CA, UNITED STATES
Brasch, Michael A., Gaithersburg, MD, UNITED STATES
Cheo, David, Kensington, MD, UNITED STATES
Hartley, James L., Frederick, MD, UNITED STATES
Byrd, Devon R.N., Waynesville, NC, UNITED STATES
Temple, Gary F., Washington Grove, MD, UNITED STATES
Invitrogen Corporation (U.S. corporation)
US 2003186233 A1 20031002
APPLICATION: US 2001-5876 A1 20011207 (10)
PRIORITY: US 2000-254510P 20001208 (60)
US 2001-291972P 20010521 (60)
US 2001-318902P 20010914 (60)
US 2001-326092P 20010928 (60)
US 2001-333124P 20011127 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 10 OF 26 USPATFULL on STN
2003:253453 Methods and compositions for inhibition of membrane fusion-associated events including RSV transmission.
Antczak, James B., Durham, NC, United States
Delmedico, Mary K., Raleigh, NC, United States
Erickson, Joel B., Durham, NC, United States
Lambert, Dennis M., Durham, NC, United States
Sista, Prakash, Durham, NC, United States
Trimeris, Inc., Durham, NC, United States (U.S. corporation)
US 6623741 B1 20030923
APPLICATION: US 2000-515965 20000229 (9)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 11 OF 26 USPATFULL on STN
2003:197045 Screening of antiviral compounds targeted to the **HIV**-1 gp41 core structure.
Jiang, Shibo, Jackson Heights, NY, United States
Debnath, Asim K., Fort Lee, NJ, United States
New York Blood Center, Inc., New York, NY, United States (U.S. corporation)
US 6596497 B1 20030722
APPLICATION: US 2000-525874 20000314 (9)
PRIORITY: US 1999-124907P 19990317 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 12 OF 26 USPATFULL on STN
2003:78127 Pharmaceutical composition for the treatment of viral infection.
Zhao, Xinxian, Shenzhen, CHINA
Sanjiu Medical Pharmaceutical Co., Ltd. (non-U.S. corporation)
US 2003054047 A1 20030320
APPLICATION: US 2002-172319 A1 20020613 (10)
PRIORITY: US 2001-298077P 20010615 (60)
DOCUMENT TYPE: Utility; APPLICATION.

L17 ANSWER 13 OF 26 USPATFULL on STN
2003:44343 Compositions and methods for eliciting immune responses with a secretion-directed protein.
Farrell, Patrick J., Calgary, CANADA
Gedamu, Lashitew, Clagary, CANADA
Iatrou, Kostas, Clagary, CANADA
US 2003031653 A1 20030213
APPLICATION: US 2001-925287 A1 20010808 (9)
DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 14 OF 26 USPATFULL on STN
2003:37612 Sequences for improving the efficiency of secretion of non-secreted protein from mammalian and insect cells.
Iatrou, Kostas, Calgary, CANADA
Farrell, Patrick J., Calgary, CANADA
Behie, Leo A., Calgary, CANADA
University Technologies International, Inc., Calgary, CANADA, T2L 2K7 (non-U.S. corporation)
US 2003027257 A1 20030206
APPLICATION: US 2002-83590 A1 20020227 (10)
PRIORITY: US 1997-56871P 19970821 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 15 OF 26 USPATFULL on STN
2003:10654 Molecular regulatory circuits to achieve sustained activation of genes of interest by a single stress.
Voellmy, Richard, Miami, FL, UNITED STATES
US 2003008349 A1 20030109
APPLICATION: US 2001-46420 A1 20011026 (10)
PRIORITY: US 1998-84236P 19980505 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 16 OF 26 USPATFULL on STN
2002:262237 Modifying insect cell gylcosylation pathways with baculovirus expression vectors.
Jarvis, Donald L., Laramie, WY, United States
University of Wyoming, Laramie, WY, United States (U.S. corporation)
US 6461863 B1 20021008
WO 9806835 19980219
APPLICATION: US 1999-242435 19991129 (9)
WO 1997-US14428 19970815 19991129 PCT 371 date
PRIORITY: US 1996-24078P 19960816 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 17 OF 26 USPATFULL on STN
2002:164665 Immunogen.
Haynes, Barton F., Durham, NC, UNITED STATES
Patel, Dhavalkumar D., Durham, NC, UNITED STATES
Alam, Munir, Chapel Hill, NC, UNITED STATES
Liao, Hua-Xin, Chapel Hill, NC, UNITED STATES
US 2002086283 A1 20020704
APPLICATION: US 2001-960717 A1 20010924 (9)
PRIORITY: US 2000-234327P 20000922 (60)
US 2001-285173P 20010423 (60)
US 2001-323697P 20010921 (60)
US 2001-323702P 20010921 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 18 OF 26 USPATFULL on STN
2002:115819 Fibrinogen-coated particles for therapeutic use.
Yen, Richard C. K., Yorba Linda, CA, United States
Hemosphere, Inc., Anaheim, CA, United States (U.S. corporation)
US 6391343 B1 20020521
WO 9639128 19961212
APPLICATION: US 1998-952765 19980410 (8)
WO 1996-US9458 19960604 19980410 PCT 371 date

DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 19 OF 26 USPATFULL on STN
2002:19408 Molecular regulatory circuits to achieve sustained activation of genes of interest by a single stress.
Voellmy, Richard, Miami, FL, United States
HSF Pharmaceuticals S.A., SWITZERLAND (non-U.S. corporation)
US 6342596 B1 20020129
APPLICATION: US 1999-304121 19990503 (9)
PRIORITY: US 1998-84236P 19980505 (60)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 20 OF 26 USPATFULL on STN
2000:31224 Insect sequences for improving the efficiency of secretion of non-secreted proteins in eukaryotic cells.
Iatrou, Kostas, Calgary, Canada
Farrell, Patrick J., Calgary, Canada
Behie, Leo A., Calgary, Canada
University Technologies International Inc., Calgary, Canada (non-U.S. corporation)
US 6037150 20000314
APPLICATION: US 1998-136421 19980820 (9)
PRIORITY: US 1997-56871P 19970821 (60)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 21 OF 26 USPATFULL on STN
2000:9723 Unique nucleotide and amino acid sequence and uses thereof.
Summers, Max D., Bryan, TX, United States
Braunagel, Sharon C., Bryan, TX, United States
Hong, Tao, Bryan, TX, United States
The Texas A M University System, College Station, TX, United States (U.S. corporation)
US 6017734 20000125
APPLICATION: US 1997-792832 19970130 (8)
PRIORITY: US 1995-955P 19950707 (60)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 22 OF 26 USPATFULL on STN
1999:102423 Method for making non-crosslinked protein particles for therapeutic and diagnostic use.
Yen, Richard C. K., Glendora, CA, United States
Hemosphere, Inc., Irvine, CA, United States (U.S. corporation)
US 5945033 19990831
APPLICATION: US 1996-747137 19961112 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 23 OF 26 USPATFULL on STN
1999:67160 Nucleic acids encoding tumor virus susceptibility genes.
Brojatsch, Jurgen, Jamaica Pond, MA, United States
Naughton, John, Somerville, MA, United States
Young, John A. T., Auburndale, MA, United States
President Fellows of Harvard College, Cambridge, MA, United States (U.S. corporation)
US 5912141 19990615
APPLICATION: US 1996-651579 19960522 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 24 OF 26 USPATFULL on STN
1998:24868 Non-crosslinked protein particles for therapeutic and diagnostic use

Yen, Richard C. K., Yorba Linda, CA, United States
Hemosphere, Inc., Irvine, CA, United States (U.S. corporation)
US 5725804 19980310
APPLICATION: US 1995-471650 19950606 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 25 OF 26 USPATFULL on STN
97:26904 Non-crosslinked protein particles for therapeutic and diagnostic use.
Yen, Richard C. K., Glendora, CA, United States
Hemosphere, Inc., Irvine, CA, United States (U.S. corporation)
US 5616311 19970401
APPLICATION: US 1994-212546 19940314 (8)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 26 OF 26 USPATFULL on STN
92:100940 Baculovirus dual promoter expression vector.
Summers, Max D., Bryan, TX, United States
Oker-Blom, Christian E. G., Turku, Finland
The Texas A M University System, College Station, TX, United States (U.S. corporation)
US 5169784 19921208
APPLICATION: US 1990-583392 19900917 (7)
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> file wpids

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	28.86	54.03

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INDEX ENHANCEMENTS PLEASE VISIT:
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=> s (HIV or human immunodeficiency virus)
22722 HIV
185899 HUMAN

```
          8060 IMMUNODEFICIENCY
         44745 VIRUS
          5102 HUMAN IMMUNODEFICIENCY VIRUS
                 (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)
L18      23476 (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)

=> s l18 and (HR1 and HR2)
           162 HR1
           151 HR2
L19          7 L18 AND (HR1 AND HR2)

=> d his

     (FILE 'HOME' ENTERED AT 00:59:31 ON 02 OCT 2006)

     FILE 'USPATFULL' ENTERED AT 00:59:40 ON 02 OCT 2006
                E DWYER JOHN/IN
L1           31 S E3-E11
L2            2 S L1 AND (HR1 OR HR2)
                E DELMEDICO MARY K/IN
L3            3 S E3-E4
L4            1 S L3 NOT L2

     FILE 'WPIDS' ENTERED AT 01:01:25 ON 02 OCT 2006
                E DWYER J/IN
L5           58 S E3-E12
                E E12
L6           28 S E1-E8
L7           74 S L5 OR L6
L8            2 S L7 AND (HR1 OR HR2)

     FILE 'MEDLINE' ENTERED AT 01:02:10 ON 02 OCT 2006
                E DWYER J/AU
                E E12
                E E12
                E E12
                E DWYER JOHN/AU
L9           22 S E3-E6
L10           1 S L9 AND (HR1 OR HR2)
                E DELMEDICO M K/AU
L11           2 S E3 OR E4
L12           1 S L11 NOT L10

     FILE 'USPATFULL' ENTERED AT 01:04:00 ON 02 OCT 2006
L13      47774 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L14         64 S L13 AND (HR1 AND HR2)
L15          7 S L14 AND (HR1/CLM OR HR2/CLM)
L16          0 S L15 AND AY<2003
L17         26 S L14 AND AY<2003

     FILE 'WPIDS' ENTERED AT 01:05:08 ON 02 OCT 2006
L18      23476 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L19          7 S L18 AND (HR1 AND HR2)

=> s l19 not l5
L20          6 L19 NOT L5

=> d l20,bib,1-6

L20  ANSWER 1 OF 6  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2006-194155 [20]   WPIDS
```

DNN N2006-167236 DNC C2006-064627
TI New primer combination comprising a set of bi-direction sequencing primers encompassing a region comprising the **HR1** and **HR2** domains of **HIV**-1, useful for detecting the presence or absence of a mutation in the nucleic acid of a pathogen.
DC B04 D16 S03
IN KEMP, S; UZGIRIS, A
PA (FARB) BAYER HEALTHCARE LLC
CYC 111
PI WO 2006023768 A2 20060302 (200620)* EN 67
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU LV MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2006023768 A2 WO 2005-US29618 20050819
PRAI US 2004-603337P 20040820; US 2004-603195P 20040820

L20 ANSWER 2 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2005-056024 [06] WPIDS
CR 2006-537770 [55]
DNC C2005-019210
TI Pharmaceutical composition useful for treating viral infections such as AIDS, has amino-modified polysaccharide having amino group linked to peptide composed of some basic amino acid residues.
DC A11 A96 B04 D16
IN BORKOW, G; LAPIDOT, A; VIJAYABASKAR, V
PA (BORK-I) BORKOW G; (LAPI-I) LAPIDOT A; (VIJA-I) VIJAYABASKAR V
CYC 1
PI US 2004229265 A1 20041118 (200506)* 45
ADT US 2004229265 A1 Provisional US 2003-465775P 20030428, US 2004-831224 20040426
PRAI US 2003-465775P 20030428; US 2004-831224 20040426

L20 ANSWER 3 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-806342 [80] WPIDS
DNC C2004-281501
TI Rendering a virus dependent on an inducing agent for viral entry comprises increasing the affinity between a **HR1** domain and a **HR2** domain of the envelope glycoprotein of the virus to such extent that the pairing occurs.
DC B04 D16
IN BALDWIN, C E; BERKHOUT, B
PA (MEDI-N) ACAD MEDISCH CENT AMSTERDAM
CYC 109
PI EP 1479774 A1 20041124 (200480)* EN 31
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
WO 2004104033 A2 20041202 (200480) EN
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT EP 1479774 A1 EP 2003-76521 20030520; WO 2004104033 A2 WO 2004-NL349 20040519

PRAI EP 2003-76521 20030520

L20 ANSWER 4 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2004-375438 [35] WPIDS
DNC C2004-141075
TI Conjugate useful for treating **HIV**-infected individual, comprises polymer operably bound to not less than two synthetic peptides derived from heptad repeat region of **HIV** gp41 by reactive functionality.
DC A96 B04 D16
IN BRAY, B; KANG, M; KINDER, D; LACKEY, J W; TVERMOES, N; ZHANG, H; ZHANG, Y; KANG, M C
PA (BRAY-I) BRAY B; (KANG-I) KANG M; (KIND-I) KINDER D; (LACK-I) LACKEY J W; (TVER-I) TVERMOES N; (TRIM-N) TRIMERIS INC
CYC 103
PI WO 2004029073 A2 20040408 (200435)* EN 79
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
US 2004122214 A1 20040624 (200442)
AU 2003278937 A1 20040419 (200462)
EP 1554306 A2 20050720 (200547) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
BR 2003014707 A 20050726 (200551)
CN 1684972 A 20051019 (200612)
KR 2005046780 A 20050518 (200641)
ADT WO 2004029073 A2 WO 2003-US30285 20030926; US 2004122214 A1 Provisional US 2002-414439P 20020927, US 2003-671282 20030924; AU 2003278937 A1 AU 2003-278937 20030926; EP 1554306 A2 EP 2003-770450 20030926, WO 2003-US30285 20030926; BR 2003014707 A BR 2003-14707 20030926, WO 2003-US30285 20030926; CN 1684972 A CN 2003-823021 20030926; KR 2005046780 A WO 2003-US30285 20030926, KR 2005-704391 20050315
FDT AU 2003278937 A1 Based on WO 2004029073; EP 1554306 A2 Based on WO 2004029073; BR 2003014707 A Based on WO 2004029073; KR 2005046780 A Based on WO 2004029073
PRAI US 2003-671282 20030924; US 2002-414439P 20020927

L20 ANSWER 5 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2002-061972 [08] WPIDS
DNC C2002-017633
TI New human polypeptides associated with reproduction, for treating and preventing reproductive, cell proliferative, endocrine, immune, infectious, metabolic and developmental disorders.
DC B04 D16
IN AZIMZAI, Y; HILLMAN, J L; TANG, Y T
PA (INCY-N) INCYTE GENOMICS INC; (AZIM-I) AZIMZAI Y; (HILL-I) HILLMAN J L; (TANG-I) TANG Y T
CYC 95
PI WO 2001079282 A2 20011025 (200208)* EN 97
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001053388 A 20011030 (200219)

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     EP 1272511      A2 20030108 (200311)  EN
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     US 2004053240   A1 20040318 (200421)
     JP 2004518401   W  20040624 (200442)      184
     AU 2001253388   A8 20050908 (200568)
ADT  WO 2001079282 A2 WO 2001-US11858 20010411; AU 2001053388 A AU 2001-53388
     20010411; EP 1272511 A2 EP 2001-926880 20010411, WO 2001-US11858 20010411;
     US 2004053240 A1 WO 2001-US11858 20010411, US 2002-257898 20021015; JP
     2004518401 W JP 2001-576877 20010411, WO 2001-US11858 20010411; AU
     2001253388 A8 AU 2001-253388 20010411
FDT  AU 2001053388 A Based on WO 2001079282; EP 1272511 A2 Based on WO
     2001079282; JP 2004518401 W Based on WO 2001079282; AU 2001253388 A8 Based
     on WO 2001079282
PRAI US 2000-197767P      20000414; US 2002-257898       20021015

L20  ANSWER 6 OF 6  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2001-514829 [56]   WPIDS
DNC  C2001-153937
TI   Heptad repeat region peptide analogs useful for inhibiting virus/cells
     fusion, useful for treating HIV and Respiratory Syncytial Virus infection.
DC   B04
IN   ANTCZAK, J B; DELMEDICO, M K; ERICKSON, J B; LAMBERT, D M; SISTA, P
PA   (TRIM-N) TRIMERIS INC
CYC  94
PI   WO 2001064013   A2 20010907 (200156)* EN  584
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
            LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
            SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001036753   A  20010912 (200204)
     US 6623741      B1 20030923 (200364)
ADT  WO 2001064013 A2 WO 2001-US3988 20010207; AU 2001036753 A AU 2001-36753
     20010207; US 6623741 B1 US 2000-515965 20000229
FDT  AU 2001036753 A Based on WO 2001064013
PRAI US 2000-515965       20000229


=> d l20,bib,ab,1-6

L20  ANSWER 1 OF 6  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN   2006-194155 [20]   WPIDS
DNN  N2006-167236       DNC C2006-064627
TI   New primer combination comprising a set of bi-direction sequencing primers
     encompassing a region comprising the HR1 and HR2 domains of HIV-1,
     useful for detecting the presence or absence of a mutation in the nucleic
     acid of a pathogen.
DC   B04 D16 S03
IN   KEMP, S; UZGIRIS, A
PA   (FARB) BAYER HEALTHCARE LLC
CYC  111
PI   WO 2006023768   A2 20060302 (200620)* EN   67
        RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT
            KE LS LT LU LV MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ
            UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE
            DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG
            KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI
```

NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

ADT WO 2006023768 A2 WO 2005-US29618 20050819

PRAI US 2004-603337P 20040820; US 2004-603195P 20040820

AB WO2006023768 A UPAB: 20060323

NOVELTY - A primer combination comprising a set of bi-direction sequencing primers encompassing a region comprising the **HR1** and **HR2** domains of **HIV-1**, is new.

DETAILED DESCRIPTION - The primer combination comprises:

(a) a forward primer selected from the group consisting of one or more of SEQ ID Nos. 2-14, all given in the specification, or their fragments of 15 or more nucleotides; and

(b) a reverse primer selected from SEQ ID Nos. 15-30, all given in the specification, and their fragment of 15 or more nucleotides.

INDEPENDENT CLAIMS are also included for:

(1) detecting the presence or absence of a mutation of interest in the nucleic acid of a pathogen, where the mutation of interest is located adjacent to a length polymorphism defining multiple quasispecies of the pathogen, comprising: obtaining from the patient sample a double-stranded DNA template encompassing the mutation of interest; sequencing a first strand of a region of the DNA template containing the mutation of interest; sequencing a second strand of a region of the DNA template containing the mutation of interest, where the region of the DNA template sequenced that is common to the first strand and second strand excludes the length polymorphism; and comparing the sequence of the first strand with the sequence of the second strand to obtain complementary strand confirmation of the sequence of the mutation of interest; and

(2) a kit for detecting the presence or absence of a mutation of interest in a pathogen in a sample containing multiple quasispecies of the pathogen having mixed length polymorphisms, where the mutation of interest is located adjacent to the length polymorphism, comprising a first primer for sequencing a first strand of a region of a DNA template containing the mutation of interest and a second primer for sequencing a second strand of a region of the DNA template containing the mutation of interest, where the region defined by the first primer and second primer excludes the length polymorphism.

USE - The primer combination, method and kit are useful for detecting the presence or absence of a mutation of interest in the nucleic acid of a pathogen, where the mutation of interest is located adjacent to a length polymorphism defining multiple quasispecies of the pathogen (claimed).

Dwg.0/0

L20 ANSWER 2 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 2005-056024 [06] WPIDS

CR 2006-537770 [55]

DNC C2005-019210

TI Pharmaceutical composition useful for treating viral infections such as AIDS, has amino-modified polysaccharide having amino group linked to peptide composed of some basic amino acid residues.

DC A11 A96 B04 D16

IN BORKOW, G; LAPIDOT, A; VIJAYABASKAR, V

PA (BORK-I) BORKOW G; (LAPI-I) LAPIDOT A; (VIJA-I) VIJAYABASKAR V

CYC 1

PI US 2004229265 A1 20041118 (200506)* 45

ADT US 2004229265 A1 Provisional US 2003-465775P 20030428, US 2004-831224 20040426

PRAI US 2003-465775P 20030428; US 2004-831224 20040426

AB US2004229265 A UPAB: 20060825

NOVELTY - A pharmaceutical composition (I), comprising as an active ingredient, an amino-modified polysaccharide having at least one amino group linked to a peptide composed of at least two basic amino acid

residues, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pentaargininamido-paromomycin conjugate (ParomR5);

(2) an argininamido-paramomycin conjugate (ParomR1) of formula (I);

(3) a tetraargininamido-neamine conjugate;

(4) an argininamido-neamine conjugate (NeamR1) of formula (II);

(5) a diargininamido-neomycin B conjugate (NeoR2) of formula (III);

(6) an argininamido-neomycin B conjugate (NeoR1) having formula (IV) or (V);

(7) selectively protecting (M1) an alkyl amino group of a polyamino cyclic compound, comprising attaching an N-protecting group to the alkyl amino group of the polyamino cyclic compound, the N-protecting group having a size selected suitable for selectively reacting with the alkyl amino group, to thus selectively protect the alkyl amino group of the polyamino cyclic compound;

(8) generating (M2) a saccharide-chemical moiety site specific conjugate, by:

(a) providing a saccharide having a reactive alkyl amino group and protected non-alkyl amino reactive groups; and

(b) reacting the saccharide with a chemical moiety;

(9) identifying (M3) a potent anti **HIV** agent, by:

(a) providing several putative anti **HIV** agents; and

(b) identifying an anti **HIV** agent of the several putative anti **HIV** agents incapable of inducing mutational instability in a predetermined sequence region of gp120, gp41 and/or CXCR4; and

(10) generating (M4) an oligo-saccharide, by:

(a) providing at least two saccharides each having at least one reactive alkyl amino group and protected non-alkyl amino reactive group; and

(b) reacting at least two saccharides.

ACTIVITY - Anti-**HIV**; Antiinflammatory; Hepatotropic; Virucide; Antibacterial; Antitubercular; Tuberculostatic.

MECHANISM OF ACTION - Binds to viral target such as Rev responsive element (RRE); Inhibitor of viral proliferation.

The ability of viral inhibition by aminoglycoside-arginine conjugates (AACs) was determined by incubating cMAG1 **HIV**-1 reporter cells with 0.2-0.5 multiplicity of infections of **HIV**-1(IIIB) for 4 days at 37 deg. C in the presence or absence of various concentration of AACs, prior to counting the number of **HIV**-1 infected cells. The presence of R3G or NeoR6 inhibited viral proliferation through viral infection, but more importantly through the first two hours of viral infection, indicating that the AACs inhibited the first stages of **HIV**-1 infectivity, and/or that the AACs were taken readily into the cells, and inhibited subsequent viral infectivity steps.

USE - (I) is useful for treating a viral infection in a subject (claimed). (I) is useful for treating viral infections such as AIDS, infections caused by equine infectious anemia virus and hepatitis C viral infections, and bacterial infections such as infections caused by aerobic gram-negative bacteria such as Bacilli such as Pseudomonas, and gram-positive bacteria such as Mycobacteria which causes tuberculosis-like diseases.

ADVANTAGE - The amino modified polysaccharides of (I) displays improved therapeutic efficacy.

DESCRIPTION OF DRAWING(S) - The figure shows inhibitory effects of NeoR6 and R3G on replication of **HIV**-1 clade C in MT2 cells.

7a, 7b/14

L20 ANSWER 3 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 2004-806342 [80] WPIDS

DNC C2004-281501

TI Rendering a virus dependent on an inducing agent for viral entry comprises increasing the affinity between a **HR1** domain and a **HR2** domain of the envelope glycoprotein of the virus to such extent that the pairing occurs.
DC B04 D16
IN BALDWIN, C E; BERKHOUT, B
PA (MEDI-N) ACAD MEDISCH CENT AMSTERDAM
CYC 109
PI EP 1479774 A1 20041124 (200480)* EN 31
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
WO 2004104033 A2 20041202 (200480) EN
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT EP 1479774 A1 EP 2003-76521 20030520; WO 2004104033 A2 WO 2004-NL349 20040519
PRAI EP 2003-76521 20030520
AB EP 1479774 A UPAB: 20041213
NOVELTY - Rendering a virus dependent on an inducing agent for viral entry by means of a pairing of two domains (**HR1** and **HR2**) of an envelope glycoprotein into a host cell, where the inducing agent is capable of interfering in the pairing.

DETAILED DESCRIPTION - Rendering a virus dependent on an inducing agent for viral entry by means of a pairing of two domains (**HR1** and **HR2**) of an envelope glycoprotein into a host cell, where the inducing agent is capable of interfering in the pairing, comprises increasing the affinity between a **HR1** domain and a **HR2** domain of the envelope glycoprotein of the virus to such extent that the pairing occurs without the presence of a host cell (a premature switch) when the inducing agent is essentially not present.

INDEPENDENT CLAIMS are included for the following:

(1) a virus dependent on an inducing agent for viral entry obtainable by the novel method;

(2) a viral replicon comprising a nucleic acid sequence with a mutation in a region encoding a **HR1** domain and/or **HR2** domain of an envelope glycoprotein, resulting in an increased affinity between the **HR1** domain and the **HR2** domain to such extent that pairing of the **HR1** and **HR2** domains occurs without the presence of a host cell when an inducing agent is essentially not present;

(3) a method for producing a virus dependent on an inducing agent for viral entry, comprising providing a permissive cell with the virus and/or a viral replicon; culturing the cell; and harvesting the dependent virus from the culture;

(4) a vaccine comprising the virus and/or viral replicon;

(5) a kit of parts comprising the virus and/or viral replicon, and an amount of inducing agent;

(6) a method for the controlled replication of the virus and/or viral replicon comprising providing a permissive cell with the virus and/or replicon; culturing the cell in the presence of the inducing agent and manipulating the amount of inducing agent present;

(7) a method for the prophylaxis of AIDS by administering the vaccine or kit to a patient; and allowing for viral entry for a limited time by providing the inducing agent;

(8) a method for modifying the virus and/or viral replicon by generating the virus and/or viral replicon; providing cells, permissive for replication of the virus and/or replicon with the virus and/or replicon; culturing the cells under conditions that allow replication of the virus and/or replicon; obtaining replicated virus and/or replicon from

the culture;

(9) a viral nucleic acid sequence comprising a mutation in a region encoding a **HR1** domain and/or **HR2** domain of an envelope glycoprotein resulting in an increased affinity between the **HR1** domain and the **HR2** domain to such extent that pairing of the **HR1** and **HR2** domains occurs when an inducing agent is essentially not present;

(10) an isolated or recombinant proteinaceous molecule capable of specifically binding the virus; and

(11) a cell comprising the replicon, or the nucleic acid.

USE - The method is useful for rendering a virus dependent on an inducing agent for viral entry by means of a pairing of two domains (**HR1** and **HR2**) of an envelope glycoprotein into a host cell (claimed).

Dwg.0/9

L20 ANSWER 4 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

Full Text

AN 2004-375438 [35] WPIDS

DNC C2004-141075

TI Conjugate useful for treating **HIV**-infected individual, comprises polymer operably bound to not less than two synthetic peptides derived from heptad repeat region of **HIV** gp41 by reactive functionality.

DC A96 B04 D16

IN BRAY, B; KANG, M; KINDER, D; LACKEY, J W; TVERMOES, N; ZHANG, H; ZHANG, Y; KANG, M C

PA (BRAY-I) BRAY B; (KANG-I) KANG M; (KIND-I) KINDER D; (LACK-I) LACKEY J W; (TVER-I) TVERMOES N; (TRIM-N) TRIMERIS INC

CYC 103

PI WO 2004029073 A2 20040408 (200435)* EN 79

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

US 2004122214 A1 20040624 (200442)

AU 2003278937 A1 20040419 (200462)

EP 1554306 A2 20050720 (200547) EN

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

BR 2003014707 A 20050726 (200551)

CN 1684972 A 20051019 (200612)

KR 2005046780 A 20050518 (200641)

ADT WO 2004029073 A2 WO 2003-US30285 20030926; US 2004122214 A1 Provisional US 2002-414439P 20020927, US 2003-671282 20030924; AU 2003278937 A1 AU 2003-278937 20030926; EP 1554306 A2 EP 2003-770450 20030926, WO 2003-US30285 20030926; BR 2003014707 A BR 2003-14707 20030926, WO 2003-US30285 20030926; CN 1684972 A CN 2003-823021 20030926; KR 2005046780 A WO 2003-US30285 20030926, KR 2005-704391 20050315

FDT AU 2003278937 A1 Based on WO 2004029073; EP 1554306 A2 Based on WO 2004029073; BR 2003014707 A Based on WO 2004029073; KR 2005046780 A Based on WO 2004029073

PRAI US 2003-671282 20030924; US 2002-414439P 20020927

AB WO2004029073 A UPAB: 20040603

NOVELTY - A conjugate (I) comprising a polymer operably bound to not less than 2 synthetic peptides, where each peptide is operably bound to polymer by a reactive functionality, comprises sequence derived from a heptad repeat region of **HIV** gp41, and comprises sequence of not less than 16 amino acids and not more than 60 amino acids, and where (I) has durability comprising antiviral activity against **HIV** strains resistant to synthetic peptide alone.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for

making (M1) (I), involves reacting a first molecule of synthetic peptide with a polymer in forming an intermediate comprising a first intermediate, where the first molecule of synthetic peptide operably binds to a first reactive functionality of the polymer, and reacting the intermediate comprising the first intermediate with a second molecule of synthetic peptide, where the second molecule of synthetic peptide operably binds to the intermediate comprising the first intermediate by a second reactive functionality of the polymer, in forming (I).

ACTIVITY - Anti-**HIV**. No supporting data is given.

MECHANISM OF ACTION - Inhibitor of gp41-mediated fusion of **HIV**-1 to a target cell.

USE - (I) is useful for inhibiting transmission of **HIV** to a target cell, which involves adding (I) to the virus and the cell. (I) inhibits fusion between the virus and the target cell in inhibiting infection of the cell by the virus. (I) further comprises a carrier. (I) is administered to an **HIV**-infected individual (claimed).

ADVANTAGE - (I) has the advantage of retaining substantial biological activity such as antiviral activity against **HIV**, and exhibiting durability as compared to synthetic peptide alone without being a part of (I). (I) increases the biological half-life of the synthetic peptide.

DESCRIPTION OF DRAWING(S) - The figure shows a schematic of **HIV**-1 gp41 showing the heptad repeat 1 (**HR1**) and **HR2** along with other functional regions of gp41.

Dwg.1/3

L20 ANSWER 5 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2002-061972 [08] WPIDS
DNC C2002-017633
TI New human polypeptides associated with reproduction, for treating and preventing reproductive, cell proliferative, endocrine, immune, infectious, metabolic and developmental disorders.
DC B04 D16
IN AZIMZAI, Y; HILLMAN, J L; TANG, Y T
PA (INCY-N) INCYTE GENOMICS INC; (AZIM-I) AZIMZAI Y; (HILL-I) HILLMAN J L; (TANG-I) TANG Y T
CYC 95
PI WO 2001079282 A2 20011025 (200208)* EN 97
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001053388 A 20011030 (200219)
EP 1272511 A2 20030108 (200311) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2004053240 A1 20040318 (200421)
JP 2004518401 W 20040624 (200442) 184
AU 2001253388 A8 20050908 (200568)
ADT WO 2001079282 A2 WO 2001-US11858 20010411; AU 2001053388 A AU 2001-53388 20010411; EP 1272511 A2 EP 2001-926880 20010411, WO 2001-US11858 20010411; US 2004053240 A1 WO 2001-US11858 20010411, US 2002-257898 20021015; JP 2004518401 W JP 2001-576877 20010411, WO 2001-US11858 20010411; AU 2001253388 A8 AU 2001-253388 20010411
FDT AU 2001053388 A Based on WO 2001079282; EP 1272511 A2 Based on WO 2001079282; JP 2004518401 W Based on WO 2001079282; AU 2001253388 A8 Based on WO 2001079282
PRAI US 2000-197767P 20000414; US 2002-257898 20021015
AB WO 200179282 A UPAB: 20020204
NOVELTY - An isolated human polypeptide (I) associated with reproduction

and designated as HR polypeptide (**HR1** or **HR2**), comprising a sequence (S1) of 706 or 453 amino acids, given in the specification, a naturally occurring polypeptide sequence having at least 90 % identity to S1, or a biologically active or immunogenic fragment of S1, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polynucleotide (II) encoding (I);

(2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);

(3) a cell transformed with (III);

(4) a transgenic organism comprising (III);

(5) producing (I) comprising culturing (3) and recovering (I);

(6) an isolated antibody (Ab) which specifically binds to (I);

(7) an isolated polynucleotide (IIa) comprising a sequence (S2) of 2653 or 1730 nucleotides, given in the specification, a naturally occurring polynucleotide sequence having at least 90 % identity to S2, a polynucleotide sequence complementary to the polynucleotides, or an RNA equivalent of the polynucleotides;

(8) an isolated polynucleotide (IIb) comprising at least 60 contiguous nucleotides of (IIa);

(9) detecting (IIa) in a sample, by:

(a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to (IIa) in the sample, where the probe specifically hybridizes to (IIa) under conditions such that a hybridization complex is formed between the probe and (IIa) or its fragments, and detecting the presence or absence of the hybridization complex, and optionally, if present, the amount of the complex; or

(b) amplifying the target polynucleotide or its fragment using polymerase chain reaction (PCR) amplification and detecting the presence or absence of the amplified target polynucleotide or its fragment, and optionally, if present, the amount of the amplified product;

(10) a composition (C1) comprising (I), an agonist or antagonist compound identified by using (I);

(11) preparing a polyclonal antibody with the specificity of Ab, by immunizing an animal with (I), or its immunogenic fragment, under conditions to elicit an antibody response, isolating antibodies from the animal, and screening the isolated antibodies with (I), and thus identifying a polyclonal antibody which binds specifically to (I);

(12) an antibody (Ab1) produced by (11);

(13) making a monoclonal antibody with the specificity of Ab, by:

(a) immunizing an animal with (I), or its immunogenic fragment, under conditions to elicit an antibody response;

(b) isolating antibody producing cells from the animal;

(c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;

(d) culturing the hybridoma cells; and

(e) isolating from the culture the monoclonal antibody which binds specifically to (I);

(14) a monoclonal antibody (MAb) produced by (13); and

(15) a composition (C2) comprising Ab, Ab1 or MAb.

ACTIVITY - Antiarteriosclerotic; hepatotropic; anti-**HIV**; antiinflammatory; antipsoriatic; cytostatic; antiinfertility; antithyroid; antiallergic; antianemic; antiasthmatic; virucide; dermatological; antidiabetic; osteopathic; immunosuppressive; antiulcer; antirheumatic; antiarthritic; antibacterial; fungicide; antiparasitic; nephrotropic; ophthalmological.

MECHANISM OF ACTION - Gene therapy; vaccine. No biological data is given.

USE - (I) is used for screening a compound:

(a) for effectiveness as an agonist or antagonist, by exposing a sample comprising (I) to a compound and detecting agonist or antagonist activity in the sample;

(b) that specifically binds (I), by combining (I) with a test compound and detecting binding of (I) to the test compound; and

(c) that modulates the activity of (I), by combining (I) with a test compound and comparing the activity of (I) in the presence or absence of the test compound.

A nucleic acid (II) encoding (I) is used for screening a compound for effectiveness in altering expression of a target polynucleotide comprising S2, by exposing a sample comprising the target polynucleotide to a compound, detecting altered expression of the target polynucleotide, and comparing the expression of the target polynucleotide in the absence or presence of varying amounts of the compound. Nucleic acid (IIb) is used for assessing toxicity of a test compound, by treating a biological sample containing nucleic acids with the test compound, hybridizing the nucleic acids of the treated biological sample with (IIb), quantifying the amount of hybridization complex formed, and comparing the amount of the complex in treated or untreated biological samples. An antibody (Ab) to (I) is used in a diagnostic test for a condition or a disease associated with the expression of HR in a biological sample, by combining the biological sample with Ab, and detecting an antibody:polypeptide complex formed. Ab is useful for detecting (I) in a sample, by incubating Ab with a sample and detecting specific binding. Ab is also used for purifying (I) from a sample, by incubating Ab with a sample, separating the antibody from the sample and obtaining the purified (I). A composition comprising an antagonist is useful for treating a disease or condition associated with decreased or increased expression of functional HR. A composition comprising an antibody is useful for diagnosing a condition or disease associated with the expression of HR in a subject (all claimed). (I) and (II) are useful for diagnosing, treating and preventing cell proliferative (e.g. arteriosclerosis, atherosclerosis, hepatitis, psoriasis and cancers), reproductive (e.g. infertility, endometriosis, ovarian tumor, and ectopic pregnancy), endocrine (e.g. disorders associated with hypopituitarism (diabetes insipidus), hyperpituitarism (acromegaly), hypothyroidism (goiter), hyperthyroidism (Grave's disease), hyperparathyroidism (Conn disease), pancreatic (diabetes mellitus), adrenal (Addison's disease), and gonadal (amenorrhea)), immune (e.g. inflammation, anemia, asthma, atopic dermatitis, acquired immunodeficiency syndrome (AIDS), hepatitis, rheumatoid arthritis, irritable bowel syndrome, osteoporosis, psoriasis, and ulcerative colitis), infectious including viral, bacterial, fungal and parasitic, metabolic (e.g. cystic fibrosis), and developmental disorders (e.g. renal tubular acidosis, Cushing's syndrome, Duchenne and Becker muscular dystrophy, seizure disorders, congenital glaucoma and cataract). (II) is used for creating knockin humanized animals or transgenic animals to model human diseases. (II) is also used in somatic or germline gene therapy. (II) is used for detecting differences in the chromosomal location due to translocation, inversion, etc., among normal, carrier or affected individuals. (II) is used as hybridization probes for mapping naturally occurring genomic sequences. (I) is used in a number of drug screening techniques.
Dwg.0/0

L20 ANSWER 6 OF 6 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN
Full Text
AN 2001-514829 [56] WPIDS
DNC C2001-153937
TI Heptad repeat region peptide analogs useful for inhibiting virus/cells fusion, useful for treating **HIV** and Respiratory Syncytial Virus infection.
DC B04
IN ANTCZAK, J B; DELMEDICO, M K; ERICKSON, J B; LAMBERT, D M; SISTA, P
PA (TRIM-N) TRIMERIS INC
CYC 94
PI WO 2001064013 A2 20010907 (200156)* EN 584
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001036753 A 20010912 (200204)
US 6623741 B1 20030923 (200364)
ADT WO 2001064013 A2 WO 2001-US3988 20010207; AU 2001036753 A AU 2001-36753 20010207; US 6623741 B1 US 2000-515965 20000229
FDT AU 2001036753 A Based on WO 2001064013
PRAI US 2000-515965 20000229
AB WO 200164013 A UPAB: 20011001

NOVELTY - Isolated heptad repeat region analog peptides (designated DP178 and DP107) comprising amino acid sequence selected from (A1)-(A9) (given in the specification) , are new. DP178 and DP107 correspond to amino acids 638-673 and 558-595 of **HIV**-1LAI transmembrane protein gp41 (heptad repeat region **HR2** and **HR1**), respectively.

DETAILED DESCRIPTION - An isolated peptide comprising an amino acid sequence selected from (A1)-(A9).

INDEPENDENT CLAIMS are also included for the following:

(1) a method (II) for inhibiting Respiratory Syncytial Virus (RSV) infection in a cell, comprising contacting the cell with a peptide comprising (A1)-(A9) (i.e. (I)) so that infection is inhibited;

(2) a method (III) for identifying a compound that inhibits formation or disrupts a DP107-like/DP178-like complex, comprising:

(a) contacting, in the presence and absence of a test compound:

(i) a peptide comprising a DP178-like amino acid sequence; and

(ii) a second peptide comprising (A1)-(A9) (i.e. (I)); and

(b) determining the binding affinity of the first peptide for the second peptide both in the presence and in the absence of the test compound (a lower binding affinity in the presence of the test compound indicates that the test compound inhibits formation of a DP107-like/DP178-like complex).

X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSK-Z (A1)
X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYI-Z (A2)
X-VLHLEGEVNKIKSALLSINKAVVSLSNGVSVLTSKVLDLKNYID-Z (A3)
X-VLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDK-Z (A4)
X-VLHLEGEVNKIKSALLSINKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z (A5)
X-SKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z (A6)
X-AVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQ-Z (A7)
X-AVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQL-Z (A8)
X-SGVAAVSKVLHLEGEVNKIKSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIIDKQL-Z (A9)

X = an amino group, an acetyl group, a 9-flurenylmethoxy-carbonyl group, a hydrophobic group or a macromolecular carrier group; and

Z = a carboxy group, an amido group, a hydrophobic group or a macromolecular carrier group.

ACTIVITY - Virucidal.

MECHANISM OF ACTION - The peptide analogs interfere with DP107-like/DP178-like complexes and therefore prevent the virus fusing with the host cell.

An antiviral assay was conducted by adding test peptides in 3% Eagle's Minimal Essential Medium (EMEM) and 100/well RSV-infected Hep-2 cells to wells containing uninfected Hep-2 cells. The well were then incubated at 37 deg. C for 48 hours. After incubation cells in control wells were checked for fusion centers. Media was removed from the wells, followed by addition, to each well, of 50 micro g 25% Crystal Violet stain in methanol. The cells were rinsed immediately and allowed to dry. The number of syncytia were then counted using a dissecting microscope. The IC50 values obtained indicated that the peptides tested, T1584, T1623, T1583 and T1581 were potent inhibitors of RSV with IC50 values of 0.23, 0.8, 1.09, 3.36 micro g/ml, respectively.

USE - The peptides may be used to inhibit Respiratory Syncytial Virus

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     (RSV) infection in a cell (claimed). They may also be used to inhibit
     HIV infection.
     Dwg.0/34


=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      55.40     109.43

FILE 'MEDLINE' ENTERED AT 01:06:06 ON 02 OCT 2006

 FILE LAST UPDATED: 30 Sep 2006 (20060930/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s (HIV or human immunodeficiency virus)
        163348 HIV
       1420903 HUMAN
        124822 IMMUNODEFICIENCY
        419508 VIRUS
         49412 HUMAN IMMUNODEFICIENCY VIRUS
                 (HUMAN(W)IMMUNODEFICIENCY(W)VIRUS)
L21     168740 (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)

=> s l21 and (HR1 and HR2)
           250 HR1
           202 HR2
L22         38 L21 AND (HR1 AND HR2)

=> d his

     (FILE 'HOME' ENTERED AT 00:59:31 ON 02 OCT 2006)

     FILE 'USPATFULL' ENTERED AT 00:59:40 ON 02 OCT 2006
                E DWYER JOHN/IN
L1           31 S E3-E11
L2            2 S L1 AND (HR1 OR HR2)
                E DELMEDICO MARY K/IN
L3            3 S E3-E4
L4            1 S L3 NOT L2

     FILE 'WPIDS' ENTERED AT 01:01:25 ON 02 OCT 2006
                E DWYER J/IN
L5           58 S E3-E12
```

```
                E E12
L6            28 S E1-E8
L7            74 S L5 OR L6
L8             2 S L7 AND (HR1 OR HR2)

     FILE 'MEDLINE' ENTERED AT 01:02:10 ON 02 OCT 2006
                E DWYER J/AU
                E E12
                E E12
                E E12
                E DWYER JOHN/AU
L9            22 S E3-E6
L10            1 S L9 AND (HR1 OR HR2)
                E DELMEDICO M K/AU
L11            2 S E3 OR E4
L12            1 S L11 NOT L10

     FILE 'USPATFULL' ENTERED AT 01:04:00 ON 02 OCT 2006
L13        47774 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L14           64 S L13 AND (HR1 AND HR2)
L15            7 S L14 AND (HR1/CLM OR HR2/CLM)
L16            0 S L15 AND AY<2003
L17           26 S L14 AND AY<2003

     FILE 'WPIDS' ENTERED AT 01:05:08 ON 02 OCT 2006
L18        23476 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L19            7 S L18 AND (HR1 AND HR2)
L20            6 S L19 NOT L5

     FILE 'MEDLINE' ENTERED AT 01:06:06 ON 02 OCT 2006
L21       168740 S (HIV OR HUMAN IMMUNODEFICIENCY VIRUS)
L22           38 S L21 AND (HR1 AND HR2)

=> s l22 not l9
L23           37 L22 NOT L9

=> d l23,cbib,ab,1-37

L23  ANSWER 1 OF 37     MEDLINE on STN
2006280992.    PubMed ID: 16709850.   HIV-1 adapts to a retrocyclin with
     cationic amino acid substitutions that reduce fusion efficiency of gp41.
     Cole Amy L; Yang Otto O; Warren Andrew D; Waring Alan J; Lehrer Robert I;
     Cole Alexander M. (Department of Molecular Biology and Microbiology,
     Burnett College of Biomedical Sciences, University of Central Florida, FL
     32816, USA.. acole@mail.ucf.edu) . Journal of immunology (Baltimore, Md. :
     1950), (2006 Jun 1) Vol. 176, No. 11, pp. 6900-5. Journal code: 2985117R.
     ISSN: 0022-1767. Pub. country: United States. Language: English.
AB   Retrocyclin (RC)-101 is a cationic theta-defensin that inhibits HIV-1
     entry. Passaging HIV-1(BAL) under selective pressure by this cyclic
     minidefensin resulted in only a 5- to 10-fold decrease in viral
     susceptibility to RC-101. Emergent viral isolates had three amino acid
     substitutions in their envelope glycoprotein. One was in a CD4-binding
     region of gp120, and the others were in the heptad repeat (HR) domains of
     gp41 (HR1 and HR2). Each mutation replaced an electroneutral or
     electronegative residue with one that was positively charged. These
     mutations were evaluated either alone or in combination in a single-round
     viral entry assay. Although the mutation in gp120 did not affect viral
     entry, the mutation in HR1 of gp41 conferred relative resistance to
     RC-101. Interestingly, the envelope with the HR2 mutation was less
     efficient and became codependent on the presence of RC-101 for entry. The
     adaptive response of HIV-1 to this cationic host defense peptide
     resembles the responses of bacteria that modulate their surface or
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membrane charge to evade analogous host defense peptides. These findings also suggest that interactions between theta-defensins and gp41 may contribute to the ability of these cyclic minidefensins to prevent **HIV**-1 entry into target cells.

L23 ANSWER 2 OF 37 MEDLINE on STN

2006216877. PubMed ID: 16623640. Susceptibility to antiretroviral drugs of CRF01_AE, CRF02_AG, and subtype C viruses from untreated patients of Africa and Asia: comparative genotypic and phenotypic data. Fleury Herve J; Toni Thomas; Lan N T H; Hung P V; Deshpande Alaka; Recordon-Pinson Patricia; Boucher Sebastien; Lazaro Estibaliz; Jauvin Valerie; Lavignolle-Aurillac Valerie; Lebel-Binay Sophie; Cheret Arnaud; Masquelier Bernard. (Laboratoire de Virologie UPRES EA 2968, Universite de Bordeaux 2, 33076 Bordeaux France.. herve.fleury@chu-bordeaux.fr) . AIDS research and human retroviruses, (2006 Apr) Vol. 22, No. 4, pp. 357-66. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Non-B **HIV**-1 viruses are predominant in developing countries where access to antiretroviral drugs (ARVs) is progressively being intensified. It is important to obtain more data on the susceptibility of these viruses to available ARVs. CRF01_AE, CRF02_AG, and subtype C strains of **HIV**-1 obtained from untreated patients from Vietnam, Cote d'Ivoire, and India were analyzed for their in vitro susceptibility to NRTIs, NNRTIs, PIs, and an entry inhibitor (T-20) using a recombinant viral assay (PHENOSCRIPT). The corresponding viruses, which had been previously sequenced in reverse transcriptase (RT), protease (prot), plus envelope (env) C2/V3 genes and had therefore been fully characterized, were further sequenced in env **HR1** + **HR2** regions. CRF01_AE isolates are sensitive to NRTIs and NNRTIs with the exception of one isolate that exhibits a decreased susceptibility to NNRTIs associated with a I135T substitution in RT. CRF02_AG and subtype C viruses are sensitive to NRTIs and NNRTIs but some CRF02_AG isolates tend to be resistant to abacavir, potentially related to associated substitutions of RT at positions 123 (D123N) plus 135 (I135V). Whereas all but one CRF01_AE isolates are fully susceptible to PIs, some CRF02_AG and, more frequently, some subtype C isolates are resistant to atazanavir. The role of substitutions in prot at positions of secondary resistance mutations 20, 36, 63, and 82 is raised with a potentially crucial role of the V82I substitution. Finally, all viruses tested, regardless of the CRF or subtype, are fully susceptible to T-20.

L23 ANSWER 3 OF 37 MEDLINE on STN

2006148916. PubMed ID: 16537590. Functional characterization of heptad repeat 1 and 2 mutants of the spike protein of severe acute respiratory syndrome coronavirus. Chan Woan-Eng; Chuang Chin-Kai; Yeh Shiou-Hwei; Chang Mau-Sun; Chen Steve S-L. (Institute of Biomedical Sciences, Academia Sinica, Nankang, Taipei 11529, Taiwan, Republic of China.) Journal of virology, (2006 Apr) Vol. 80, No. 7, pp. 3225-37. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB To understand the roles of heptad repeat 1(**HR1**) and **HR2** of the spike (S) protein of the severe acute respiratory syndrome coronavirus (SARS-CoV) in virus-cell interactions, the conserved Leu or Ile residues located at positions 913, 927, 941, and 955 in **HR1** and 1151, 1165, and 1179 in **HR2** were individually replaced with an alpha-helix-breaker Pro residue. The 913P mutant was expressed mainly as a faster-migrating, lower-molecular-weight S(L) form, while the wild type and all other mutants produced similar levels of both the S(L) form and the slower-migrating, higher-molecular-weight S(H) form. The wild-type S(L) form was processed to the S(H) form, whereas the S(L) form of the 913P mutant was inefficiently converted to the S(H) form after biosynthesis. None of these mutations affected cell surface expression or binding to its cognate ACE2 receptor. In a **human immunodeficiency virus** type 1/SARS S coexpression study, all mutants except the 913P mutant

incorporated the S(H) form into the virions as effectively as did the wild-type S(H) form. The mutation at Ile-1151 did not affect membrane fusion or viral entry. The impaired viral entry of the 927P, 941P, 955P, and 1165P mutants was due to their inability to mediate membrane fusion, whereas the defect in viral entry of the 1179P mutant occurred not at the stage of membrane fusion but rather at a postfusion stage. Our study demonstrates the functional importance of **HR1** and **HR2** of the SARS-CoV spike protein in membrane fusion and viral entry.

L23 ANSWER 4 OF 37 MEDLINE on STN

2006042244. PubMed ID: 16430194. Heptad-repeat-2 mutations enhance the stability of the enfuvirtide-resistant **HIV**-1 gp41 hairpin structure. Jenwitheesuk Ekachai; Samudrala Ram. (Department of Microbiology, University of Washington, School of Medicine, Seattle, WA 98195, USA.) Antiviral therapy, (2005) Vol. 10, No. 8, pp. 893-900. Journal code: 9815705. ISSN: 1359-6535. Pub. country: England: United Kingdom. Language: English.

AB Enfuvirtide (T20) is a peptide-based fusion inhibitor derived from the heptad repeat 2 (**HR2**) region of **HIV**-1 glycoprotein 41 (gp41). The inhibitor binds to the gp41 heptad repeat 1 (**HR1**) region, thereby blocking viral **HR1/HR2** association. Mutations in **HR1** have been reported to cause enfuvirtide resistance and reduce viral fitness. In this study, we first showed that scores obtained by a residue-specific all-atom probability discriminatory function (RAPDF) may be used as a reliable predictor of structural stability of gp41 mutants by comparing it to experimentally determined melting temperatures, and as a reliable indicator of enfuvirtide resistance by comparing it to experimentally determined fusion inhibition and viral fitness levels. We then generated an initial set of 28 theoretical structures of the **HR1/HR2** hairpin complex where each structure consists of one mutation on **HR1** known to cause enfuvirtide resistance and a wild-type amino acid at the corresponding **HR2** residue. Mutations were then introduced in the corresponding **HR2** residue of each structure where the wild-type amino acid was changed to each of the other nineteen amino acids. The enfuvirtide-resistant **HR1** mutants with compensatory mutations at the corresponding **HR2** residues had better RAPDF scores than those **HR1** mutants with wild-type **HR2**. This indicates that mutations in **HR2** improve structural stability of the **HR1/HR2** hairpin complex and may lead to enhanced enfuvirtide resistance when present with resistant **HR1** mutations. Modification of the amino acid side chains that contribute to enfuvirtide resistance using the RAPDF scores as a guide may help design of a second generation of fusion inhibitors against the enfuvirtide-resistant strains.

L23 ANSWER 5 OF 37 MEDLINE on STN

2005690425. PubMed ID: 16372284. Long-term monitoring of genotypic and phenotypic resistance to T20 in treated patients infected with **HIV**-1. Perez-Alvarez L; Carmona R; Ocampo A; Asorey A; Miralles C; Perez de Castro S; Pinilla M; Contreras G; Taboada J A; Najera R. (Area de Patogenia Viral, Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain.) Journal of medical virology, (2006 Feb) Vol. 78, No. 2, pp. 141-7. Journal code: 7705876. ISSN: 0146-6615. Pub. country: United States. Language: English.

AB The aim of this study was to investigate the susceptibility to T20 and the dynamics of amino acid changes in **HR1** and **HR2** of gp41 of **HIV**-1 obtained from plasma, peripheral blood mononuclear cells (PBMC), and primary isolates (PI) in four highly antiretroviral-experienced patients. These patients received T20 plus an antiretroviral regimen and were followed-up over a period of 40-72 weeks. In one non-responder patient, N43D substitution was detected at 12 weeks of treatment, in association with a value of T20-IC50 of 10 microg/ml (10-fold increase). Double mutations N42T + N43D were observed in plasma RNA at 32 weeks and remained

detectable up to 16 weeks after the withdrawal of the drug. The S138A substitution in **HR2** was observed in plasma RNA at 32 weeks, and both in plasma RNA and in PI DNA at 40 weeks, associated with an increase of the T20-IC50 to 25 microg/ml (25-fold increase). Mutations V101G and E137K, not reported previously, were also observed in the **HR2** region. Whether these new substitutions play a role in T20 resistance needs to be examined. In three temporary responders, coinciding with viral load rebound, G36D, and N42T substitutions were observed at 12, 24, and 40 weeks. G36D mutation was associated with a value of T20-IC50 of 5 microg/ml. The **HR2** S138A mutation was detected after the detection of **HR1** substitutions and was associated with an increase in the level of T20-IC50 to 125 microg/ml (125-fold increase) All these data reinforce the role of gp41 amino acids 36-45 and the potential influence of the **HR2** S138A mutation in the genotypic/phenotypic resistance to T20.

L23 ANSWER 6 OF 37 MEDLINE on STN

2005671901. PubMed ID: 16290276. Why are **HIV**-1 fusion inhibitors not effective against SARS-CoV? Biophysical evaluation of molecular interactions. Veiga Salome; Yuan Yunyun; Li Xuqin; Santos Nuno C; Liu Gang; Castanho Miguel A R B. (Centro de Quimica e Bioquimica, Faculdade de Ciencias da Universidade de Lisboa, Campo Grande C8, 1749-016 Lisboa, Portugal.) Biochimica et biophysica acta, (2006 Jan) Vol. 1760, No. 1, pp. 55-61. Electronic Publication: 2005-10-28. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB The envelope spike (S) glycoprotein of the severe acute respiratory syndrome associated coronavirus (SARS-CoV) mediates the entry of the virus into target cells. Recent studies point out to a cell entry mechanism of this virus similar to other enveloped viruses, such as **HIV**-1. As it happens with other viruses peptidic fusion inhibitors, SARS-CoV S protein **HR2**-derived peptides are potential therapeutic drugs against the virus. It is believed that **HR2** peptides block the six-helix bundle formation, a key structure in the viral fusion, by interacting with the **HR1** region. It is a matter of discussion if the **HIV**-1 gp41 **HR2**-derived peptide T20 (enfuvirtide) could be a possible SARS-CoV inhibitor given the similarities between the two viruses. We tested the possibility of interaction between both T20 (**HIV**-1 gp41 **HR2**-derived peptide) and T-1249 with S protein **HR1**- and **HR2**-derived peptides. Our biophysical data show a significant interaction between a SARS-CoV **HR1**-derived peptide and T20. However, the interaction is only moderate (K(B)=(1.1+/-0.3)x10(5) M(-1)). This finding shows that the reasoning behind the hypothesis that T20, already approved for clinical application in AIDS treatment, could inhibit the fusion of SARS-CoV with target cells is correct but the effect may not be strong enough for application.

L23 ANSWER 7 OF 37 MEDLINE on STN

2005665310. PubMed ID: 16352560. Expanded tropism and altered activation of a retroviral glycoprotein resistant to an entry inhibitor peptide. Amberg Sean M; Netter Robert C; Simmons Graham; Bates Paul. (Department of Microbiology, University of Pennsylvania School of Medicine, 225 Johnson Pavilion, 3610 Hamilton Walk, Philadelphia, PA 19104-6076, USA.) Journal of virology, (2006 Jan) Vol. 80, No. 1, pp. 353-9. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The envelope of class I viruses can be a target for potent viral inhibitors, such as the **human immunodeficiency virus** type 1 (**HIV**-1) inhibitor enfuvirtide, which are derived from the C-terminal heptad repeat (**HR2**) of the transmembrane (TM) subunit. Resistance to an **HR2**-based peptide inhibitor of a model retrovirus, subgroup A of the Avian Sarcoma and Leukosis Virus genus (ASLV-A), was studied by examining mutants derived by viral passage in the presence of inhibitor. Variants with reduced sensitivity to inhibitor were readily selected in vitro. Sensitivity determinants were identified for 13 different isolates, all of

which mapped to the TM subunit. These determinants were identified in two regions: (i) the N-terminal heptad repeat (**HR1**) and (ii) the N-terminal segment of TM, between the subunit cleavage site and the fusion peptide. The latter class of mutants identified a region outside of the predicted **HR2**-binding site that can significantly alter sensitivity to inhibitor. A subset of the **HR1** mutants displayed the unanticipated ability to infect nonavian cells. This expanded tropism was associated with increased efficiency of envelope triggering by soluble receptor at low temperatures, as measured by protease sensitivity of the surface subunit (SU) of envelope. In addition, expanded tropism was linked for the most readily triggered mutants with increased sensitivity to neutralization by SU-specific antiserum. These observations depict a class of **HR2** peptide-selected mutations with a reduced activation threshold, thereby allowing the utilization of alternative receptors for viral entry.

L23 ANSWER 8 OF 37 MEDLINE on STN

2005621192. PubMed ID: 16302461. Enfuvirtide, the first fusion inhibitor to treat **HIV** infection. Poveda Eva; Briz Veronica; Soriano Vincent. (Department of Infectious Diseases, Hospital Carlos III, Madrid, Spain.) AIDS reviews, (2005 Jul-Sep) Vol. 7, No. 3, pp. 139-47. Ref: 71. Journal code: 101134876. ISSN: 1139-6121. Pub. country: Spain. Language: English.

AB Entry inhibitors are a new class of drugs for the treatment of **HIV** infection. Enfuvirtide is the first compound of this family to be approved for clinical use. It blocks **HIV** fusion to host cells. It is a synthetic peptide that mimics an **HR2** fragment of gp41, blocking the formation of a six-helix bundle structure which is critical in the fusion process. Enfuvirtide is a good therapeutic option as rescue therapy in combination with other active antiretrovirals and works against different **HIV**-1 variants, including all group M subtypes and group O. However, it is not active against **HIV**-2. The main mechanism of resistance to enfuvirtide depends of the selection of changes in a 10-amino acid domain between residues 36 to 45 in the **HR1** region of gp41. Single and double mutations in this region have been shown to result in high-level resistance to enfuvirtide. A negative impact of enfuvirtide-resistance mutations on viral fitness has been postulated, since resistance mutations tend to disappear soon after drug discontinuation and because immunologic benefits have been noticed despite virologic failure in patients undergoing enfuvirtide treatment.

L23 ANSWER 9 OF 37 MEDLINE on STN

2005617776. PubMed ID: 16253271. Design and characterization of viral polypeptide inhibitors targeting Newcastle disease virus fusion. Zhu Jieqing; Jiang Xiuli; Liu Yueyong; Tien Po; Gao George F. (Center For Molecular Virology, Institute of Microbiology, Chinese Academy of Sciences, Zhongguancun Beiyitiao, Beijing 100080, China.) Journal of molecular biology, (2005 Dec 2) Vol. 354, No. 3, pp. 601-13. Electronic Publication: 2005-10-10. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB Paramyxovirus infections can be detected worldwide with some emerging zoonotic viruses and currently there are no specific therapeutic treatments or vaccines available for many of these diseases. Recent studies have demonstrated that peptides derived from the two heptad repeat regions (**HR1** and **HR2**) of paramyxovirus fusion proteins could be used as inhibitors of virus fusion. The mechanism underlying this activity is in accordance with that of class I virus fusion proteins, of which **human immunodeficiency virus** (**HIV**) and influenza virus fusion proteins are members. For class I virus fusion proteins, the **HR1** fragment binds to **HR2** to form a six-helix bundle with three **HR1** fragments forming the central coiled bundle surrounded by three coiled **HR2** fragments in the post fusion conformational state (fusion core). It is hypothesized that the introduced exogenous **HR1** or **HR2** can compete against their endogenous counterparts, which results in fusion inhibition. Using

Newcastle disease virus (NDV) as a model, we designed several protein inhibitors, denoted HR212 as well asHR121 and 5-Helix, which could bind the **HR1** or **HR2** region of fusion protein, respectively. All the proteins were expressed and purified using a GST-fusion expression system in Escherichia coli. The HR212 or GST-HR212 protein, which binds the **HR1** peptide in vitro, displayed inhibitory activity against NDV-mediated cell fusion, while the HR121 and 5-Helix proteins, which bind the **HR2** peptide in vitro, inhibited virus fusion from the avirulent NDV strain when added before the cleavage of the fusion protein. These results showed that the designed HR212, HR121 or 5-Helix protein could serve as specific antiviral agents. These data provide additional insight into the difference between the virulent and avirulent strains of NDV.

L23 ANSWER 10 OF 37 MEDLINE on STN

2005393336. PubMed ID: 16051817. Determinants of **human immunodeficiency virus** type 1 resistance to membrane-anchored gp41-derived peptides. Lohrengel Sabine; Hermann Felix; Hagmann Isabel; Oberwinkler Heike; Scrivano Laura; Hoffmann Caroline; von Laer Dorothee; Dittmar Matthias T. (Abt. Virologie, Hygiene-Institut, Universitat Heidelberg, D-69120 Heidelberg, Germany.) Journal of virology, (2005 Aug) Vol. 79, No. 16, pp. 10237-46. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The expression of a membrane-anchored gp41-derived peptide (M87) has been shown to confer protection from infection through **human immunodeficiency virus** type 1 (**HIV**-1) (Hildinger et al., J. Virol. 75:3038-3042, 2001). In an effort to characterize the mechanism of action of this membrane-anchored peptide in comparison to the soluble peptide T-20, we selected resistant variants of **HIV**-1(NL4-3) and **HIV**-1(BaL) by serial virus passage using PM1 cells stably expressing peptide M87. Sequence analysis of the resistant isolates showed different patterns of selected point mutations in heptad repeat regions 1 and 2 (**HR1** and **HR2**, respectively) for the two viruses analyzed. For **HIV**-1(NL4-3) a single amino acid change at position 33 in **HR1** (L33S) was selected, whereas for **HIV**-1(BaL) the majority of the sequences obtained showed two amino acid changes, one in **HR1** and one in **HR2** (I48V/N126K). In both selections the most important contiguous 3-amino-acid sequence, GIV, within **HR1**, associated with resistance to soluble T-20, was not changed. Site-directed mutagenesis studies confirmed the importance of the characterized point mutations to confer resistance to M87 as well as to soluble T-20 and T-649. Replication capacity and dual-color competition assays revealed that the double mutation I48V/N126K in **HIV**-1(BaL) results in a strong reduction of viral fitness, whereas the L33S mutation in **HIV**-1(NL4-3) did enhance viral fitness compared to the respective parental viruses. However, the selected point mutations did not confer resistance to the more recently described optimized membrane-anchored fusion inhibitor M87o (Egelhofer et al., J. Virol. 78:568-575, 2004), strengthening the importance of this novel antiviral concept for gene therapy approaches.

L23 ANSWER 11 OF 37 MEDLINE on STN

2005338444. PubMed ID: 15989465. Enfuvirtide is active against **HIV** type 1 group O. Poveda Eva; Barreiro Pablo; Rodes Berta; Soriano Vincent. (Department of Infectious Diseases, Hospital Carlos III, Madrid, Spain.) AIDS research and human retroviruses, (2005 Jun) Vol. 21, No. 6, pp. 583-5. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB A high diversity within the **HR1**/**HR2** regions of viral gp41 and one natural change (N42D) within the 36-45 aa domain in **HIV**-1 group O in comparison with **HIV**-1 group M isolates have led us to suspect that enfuvirtide (ENF) should not be active against **HIV**-1 group O. We analyzed in vitro and in vivo the antiviral activity of ENF against **HIV**-1 group O isolates. The IC50 at baseline was 0.15 +/- 0.028

microg/ml in a clinically derived virus specimen. After initiating treatment with ENF, a significant decline in plasma **HIV**-RNA and CD4 gain was noticed in one patient. Therefore, individuals with **HIV**-1 group O strains might benefit from ENF therapy.

L23 ANSWER 12 OF 37 MEDLINE on STN

2005330572. PubMed ID: 15950253. An alternative conformation of the gp41 heptad repeat 1 region coiled coil exists in the **human immunodeficiency virus** (**HIV**-1) envelope glycoprotein precursor. Mische Claudia C; Yuan Wen; Strack Bettina; Craig Stewart; Farzan Michael; Sodroski Joseph. (Department of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, Boston, MA 02115, USA.) Virology, (2005 Jul 20) Vol. 338, No. 1, pp. 133-43. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB The **human immunodeficiency virus** (**HIV**-1) transmembrane envelope glycoprotein, gp41, which mediates virus-cell fusion, exists in at least three different conformations within the trimeric envelope glycoprotein complex. The structures of the prefusogenic and intermediate states are unknown; structures representing the postfusion state have been solved. In the postfusion conformation, three helical heptad repeat 2 (**HR2**) regions pack in an antiparallel fashion into the hydrophobic grooves on the surface of a triple-helical coiled coil formed by the heptad repeat 1 (**HR1**) regions. We studied the prefusogenic conformation of gp41 by mutagenic alteration of membrane-anchored and soluble forms of the **HIV**-1 envelope glycoproteins. Our results indicate that, in the **HIV**-1 envelope glycoprotein precursor, the gp41 **HR1** region is in a conformation distinct from that of a trimeric coiled coil. Thus, the central gp41 coiled coil is formed during the transition of the **HIV**-1 envelope glycoproteins from the precursor state to the receptor-bound intermediate.

L23 ANSWER 13 OF 37 MEDLINE on STN

2005284642. PubMed ID: 15929708. Enfuvirtide binding domain is highly conserved in non-B **HIV** type 1 strains from Cameroon, West Central Africa. Aghokeng Avelin Fobang; Ewane Leonard; Awazi Bih; Nanfack Aubin; Delaporte Eric; Zekeng Leopold; Peeters Martine. (Laboratoire de Sante Hygiene Mobile, Yaounde, Cameroon.) AIDS research and human retroviruses, (2005 May) Vol. 21, No. 5, pp. 430-3. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Recently T-20 or enfuvirtide, the first drug of a new class of antiretrovirals targeting the entry stage of the virus life cycle, has been clinically approved. Enfuvirtide is a peptide derived from the **HR2** region of the transmembrane glycoprotein from the HXB2 **HIV**-1 subtype B prototype strain that binds to the **HR1** region. Drug resistance seems to occur in the **HR1** region between amino acids 36 and 45. We examined to what extent this region is conserved in 184 non-B strains from Cameroon: 132 (71.7%) CRF02-AG, 14 (7.6%) subtype A, 11 (5.9%) F2, 9 (4.8%) subtype D, 8 (4.3%) subtype G, 4 (2.1%) CRF01-AE, 4 (2.1%) CRF11-cpx, and 2 (1.1%) CRF06-cpx. Among the 184 strains studied, no amino acid mutation was found in the highly conserved three amino acid motif at codons 36-38 (GIV) that are important determinants of viral susceptibility to enfuvirtide. Other common substitutions like Q40H and N42T were also absent. The N42S polymorphism was present in 148 (80.4%) strains. Analysis of the **HR2** domain, from which the peptide is derived, indicated a much greater genetic variability as compared to **HR1**.

L23 ANSWER 14 OF 37 MEDLINE on STN

2005280239. PubMed ID: 15913557. Rational design of highly potent **HIV**-1 fusion inhibitory proteins: implication for developing antiviral therapeutics. Ni Ling; Gao George F; Tien Po. (Department of Molecular Virology, Institute of Microbiology, Chinese Academy of Sciences, Beijing 100080, PR China.) Biochemical and biophysical research communications,

(2005 Jul 8) Vol. 332, No. 3, pp. 831-6. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Recombinant protein containing one heptad-repeat 1 (**HR1**) segment and one **HR2** segment of the **HIV**-1 gp41 (**HR1-HR2**) has been shown to fold into thermally stable six-helix bundle, representing the fusogenic core of gp41. In this study, we have used the fusogenic core as a scaffold to design **HIV**-1 fusion inhibitory proteins by linking another **HR1** to the C terminus of **HR1-HR2** (HR121) or additional **HR2** to the N terminus of **HR1-HR2** (HR212). Both recombinant proteins could be abundantly and solubly expressed and easily purified, exhibiting high stability and potent inhibitory activity on **HIV**-1 fusion with IC50 values of 16.2+/-2.8 and 2.8+/-0.63 nM, respectively. These suggest that these rationally designed proteins can be further developed as novel anti-**HIV**-1 therapeutics.

L23 ANSWER 15 OF 37 MEDLINE on STN

2005148320. PubMed ID: 15781229. Design of recombinant protein-based SARS-CoV entry inhibitors targeting the heptad-repeat regions of the spike protein S2 domain. Ni Ling; Zhu Jieqing; Zhang Junjie; Yan Meng; Gao George F; Tien Po. (Department of Molecular Virology, Institute of Microbiology, Chinese Academy of Sciences, Beijing 100080, PR China.) Biochemical and biophysical research communications, (2005 Apr 29) Vol. 330, No. 1, pp. 39-45. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Entry of SARS-CoV into a target cell is initiated by binding of the S1 domain of spike protein to a receptor, followed by conformational changes of the spike protein S2 domain, resulting in the formation of a six-helix bundle by the heptad-repeat (**HR1** and **HR2**) regions. Our previous studies have demonstrated that peptides derived from **HR2** region could inhibit SARS-CoV entry. However, synthesis of these peptides is at high cost. In this study, we designed two recombinant proteins, one containing two **HR1** and one **HR2** peptides (denoted HR121), and the other consisting of two **HR2** and one **HR1** peptides (designated HR212). These two proteins could be easily purified with the low cost of production, exhibiting high stability and potent inhibitory activity on entry of the **HIV**/SARS pseudoviruses with IC(50) values of 4.13 and 0.95muM, respectively. These features suggest that HR121 and HR212 can serve as potent inhibitors of SARS-CoV entry.

L23 ANSWER 16 OF 37 MEDLINE on STN

2005112034. PubMed ID: 15742549. [Enfuvirtide, first fusion inhibitor in the treatment of **human immunodeficiency virus** infection: mechanism of action and pharmacokinetics]. Enfuvirtide, premier inhibiteur de fusion dans le traitement de l'infection par le virus de l'immunodeficience humaine: mecanisme d'action et pharmacocinetique. Raffi Francois. (Service des maladies infectieuses et tropicales, Hotel-Dieu CHU, place Alexis-Ricordeau, 44093 Nantes cedex 1, France.. francois.raffi@chu-nantes.fr) . Medecine et maladies infectieuses, (2004 Sep) Vol. 34 Spec No 1, pp. 3-7. Ref: 4. Journal code: 0311416. ISSN: 0399-077X. Pub. country: France. Language: French.

AB Enfuvirtide is a 36 amino-acid synthetic peptide derived from the **HR2** sequence of the **HIV**-1 gp41. Enfuvirtide is different from other antiretroviral drugs by its extra-cellular action where it binds to the **HR1** domain at the viral surface of the gp41. The drug inhibits the conformational change of the glycoprotein, preventing the intimate fusion between the **HIV** envelope and the CD4 cell membrane and finally the penetration of the viral capside into the target cells. Following a 90 mg subcutaneous injection, the plasma concentration rises rapidly to reach a 4.59 +/- 1.5 microg/ml Cmax between 5 and 7 hours. Residual concentrations are between 2.6 and 3.4 microg/ml and the bioavailability of the drug is approximately 80%. Plasma concentrations and area under curve are dose-dependant. The site of injection does not influence the

pharmacokinetic parameters of the drug. Infuvirtide is not an inhibitor of the P450 cytochrome and no pharmacokinetic interactions have been reported with P450 metabolised drugs.

L23 ANSWER 17 OF 37 MEDLINE on STN

2005106747. PubMed ID: 15737628. Characterization of BIV Env core: implication for mechanism of BIV-mediated cell fusion. Li Shu; Zhu Jieqing; Peng Yu; Cui Shanshan; Wang Chunping; Gao George F; Tien Po. (Modern Virology Research Center, State Key Laboratory of Virology, College of Life Sciences, Wuhan University, Wuhan 430072, China.) Biochemical and biophysical research communications, (2005 Apr 8) Vol. 329, No. 2, pp. 603-9. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Entry of lentiviruses, such as **human immunodeficiency virus** type 1 (**HIV**-1) and simian immunodeficiency virus (SIV), requires folding of two heptad repeat regions (**HR1** and **HR2**) of gp41 into a trimer-of-hairpins, which subsequently brings virus and cell membrane into fusion. This motif is a generalized feature of viral fusion proteins and has been exploited in generating antiviral fusion agents. In the present paper, we report structural characters of Env protein from another lentivirus, bovine immunodeficiency virus (BIV), which contributes to a good animal model of **HIV**. BIV **HR1** and **HR2** regions are predicted by two different programs and expressed separately or conjointly in Escherichia coli. Biochemical and biophysical analyses show that the predicted HRs of BIV Env can form a stable trimer-of-hairpins or six-helix bundle just like that formed by feline immunodeficiency virus Env. Cell fusion assay demonstrates that the **HR2** peptide of BIV can efficiently inhibit the virus-mediated cell fusion.

L23 ANSWER 18 OF 37 MEDLINE on STN

2005097527. PubMed ID: 15728911. Emergence and evolution of enfuvirtide resistance following long-term therapy involves heptad repeat 2 mutations within gp41. Xu L; Pozniak A; Wildfire A; Stanfield-Oakley S A; Mosier S M; Ratcliffe D; Workman J; Joall A; Myers R; Smit E; Cane P A; Greenberg M L; Pillay D. (Health Protection Agency Antiviral Suspectibility Reference Unit, Birmingham, UK.) Antimicrobial agents and chemotherapy, (2005 Mar) Vol. 49, No. 3, pp. 1113-9. Journal code: 0315061. ISSN: 0066-4804. Pub. country: United States. Language: English.

AB The objective of this study was to track the evolution of sequence changes in both the heptad region 1 (**HR1**) and **HR2** domains of gp41 associated with resistance to enfuvirtide (ENF) in a patient cohort receiving long-term ENF treatment. We studied 17 highly antiretroviral agent-experienced patients receiving long-term ENF treatment with virological rebound or a lack of suppression. Sixty-two samples obtained after between 5 and 107 weeks of ENF therapy were analyzed. Baseline samples from 15 of these 17 patients were available for analysis. Viruses from five samples from four patients were also sequenced after the cessation of ENF therapy. Drug susceptibilities were assessed by a pseudotype virus reporter assay. We identified **HR1** and **HR2** sequence changes over time in relation to the baseline sequences. Mutations in **HR1** (amino acids 36 to 45) were noted in all cases, including previously unreported changes N42Q/H and N43Q. In addition to a range of **HR2** sequence changes at polymorphic sites, isolates from 6 of 17 (35%) patients developed an S138A substitution in the **HR2** domain at least 8 weeks after the start of ENF treatment and also subsequent to the first emergence of **HR1** mutations. In most, but not all, cases the S138A mutation accompanied **HR1** mutations at position 43. Molecular modeling demonstrates the close proximity of S138A with amino acids 40 and 45 in **HR1**. Of note, isolates in samples available from four patients demonstrated the loss of both the **HR1** and the S138A **HR2** mutations following the cessation of therapy. We show that the S138A **HR2** mutation increased the level of resistance by approximately threefold over that

conferred by the **HR1** mutation N43D. Continual evolution of **HR1** in the domain from amino acids 36 to 45 was observed during long-term ENF therapy. We have identified, for the first time, an ENF resistance-associated **HR2** mutation, S138A, which appeared in isolates from 6 of 17 patients with virological failure and demonstrated its potential to contribute to drug resistance. We propose that this represents a possible secondary and/or compensatory mutation, particularly when it coexists with mutations at position 43 in HR-1.

L23 ANSWER 19 OF 37 MEDLINE on STN

2005023927. PubMed ID: 15650199. Identification of the membrane-active regions of the severe acute respiratory syndrome coronavirus spike membrane glycoprotein using a 16/18-mer peptide scan: implications for the viral fusion mechanism. Guillen Jaime; Perez-Berna Ana J; Moreno Miguel R; Villalain Jose. (Instituto de Biologia Molecular y Celular, Universidad Miguel Hernandez, E-03202 Elche-Alicante, Spain.) Journal of virology, (2005 Feb) Vol. 79, No. 3, pp. 1743-52. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB We have identified the membrane-active regions of the severe acute respiratory syndrome coronavirus (SARS CoV) spike glycoprotein by determining the effect on model membrane integrity of a 16/18-mer SARS CoV spike glycoprotein peptide library. By monitoring the effect of this peptide library on membrane leakage in model membranes, we have identified three regions on the SARS CoV spike glycoprotein with membrane-interacting capabilities: region 1, located immediately upstream of heptad repeat 1 (**HR1**) and suggested to be the fusion peptide; region 2, located between **HR1** and **HR2**, which would be analogous to the loop domain of **human immunodeficiency virus** type 1; and region 3, which would correspond to the pretransmembrane region. The identification of these membrane-active regions, which are capable of modifying the biophysical properties of phospholipid membranes, supports their direct role in SARS CoV-mediated membrane fusion, as well as facilitating the future development of SARS CoV entry inhibitors.

L23 ANSWER 20 OF 37 MEDLINE on STN

2004606996. PubMed ID: 15345712. Crystal structure of severe acute respiratory syndrome coronavirus spike protein fusion core. Xu Yanhui; Lou Zhiyong; Liu Yiwei; Pang Hai; Tien Po; Gao George F; Rao Zihe. (Laboratory of Structural Biology, Tsinghua University, Beijing 100084 and National Laboratory of Bio-Macromolecules, Institute of Biophysics, Beijing 100101, China.) The Journal of biological chemistry, (2004 Nov 19) Vol. 279, No. 47, pp. 49414-9. Electronic Publication: 2004-09-01. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB Severe acute respiratory syndrome coronavirus is a newly emergent virus responsible for a recent outbreak of an atypical pneumonia. The coronavirus spike protein, an enveloped glycoprotein essential for viral entry, belongs to the class I fusion proteins and is characterized by the presence of two heptad repeat (HR) regions, **HR1** and **HR2**. These two regions are understood to form a fusion-active conformation similar to those of other typical viral fusion proteins. This hairpin structure likely juxtaposes the viral and cellular membranes, thus facilitating membrane fusion and subsequent viral entry. The fusion core protein of severe acute respiratory syndrome coronavirus spike protein was crystallized, and the structure was determined at 2.8 A of resolution. The fusion core is a six-helix bundle with three **HR2** helices packed against the hydrophobic grooves on the surface of central coiled coil formed by three parallel **HR1** helices in an oblique antiparallel manner. This structure shares significant similarity with the fusion core structure of mouse hepatitis virus spike protein and other viral fusion proteins, suggesting a conserved mechanism of membrane fusion. Drug discovery strategies aimed at inhibiting viral entry by blocking hairpin formation, which have been successfully used in **human immunodeficiency**

virus 1 inhibitor development, may be applicable to the inhibition of severe acute respiratory syndrome coronavirus on the basis of structural information provided here. The relatively deep grooves on the surface of the central coiled coil will be a good target site for the design of viral fusion inhibitors.

L23 ANSWER 21 OF 37 MEDLINE on STN

2004571046. PubMed ID: 15518555. Characterization of the heptad repeat regions, **HR1** and **HR2**, and design of a fusion core structure model of the spike protein from severe acute respiratory syndrome (SARS) coronavirus. Xu Yanhui; Zhu Jieqing; Liu Yiwei; Lou Zhiyong; Yuan Fang; Liu Yueyong; Cole David K; Ni Ling; Su Nan; Qin Lan; Li Xu; Bai Zhihong; Bell John I; Pang Hai; Tien Po; Gao George F; Rao Zihe. (Laboratory of Structural Biology, Tsinghua University, Beijing 100084, China.) Biochemistry, (2004 Nov 9) Vol. 43, No. 44, pp. 14064-71. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB Severe acute respiratory syndrome coronavirus (SARS-CoV) is a newly emergent virus responsible for a worldwide epidemic in 2003. The coronavirus spike proteins belong to class I fusion proteins, and are characterized by the existence of two heptad repeat (HR) regions, **HR1** and **HR2**. The **HR1** region in coronaviruses is predicted to be considerably longer than that in other type I virus fusion proteins. Therefore the exact binding sequence to **HR2** from the **HR1** is not clear. In this study, we defined the region of **HR1** that binds to **HR2** by a series of biochemical and biophysical measures. Subsequently the defined **HR1** (902-952) and **HR2** (1145-1184) chains, which are different from previously defined binding regions, were linked together by a flexible linker to form a single-chain construct, 2-Helix. This protein was expressed in Escherichia coli and forms a typical six-helix coiled coil bundle. Highly conserved HR regions between mouse hepatitis virus (MHV) and SARS-CoV spike proteins suggest a similar three-dimensional structure for the two fusion cores. Here, we constructed a homology model for SARS coronavirus fusion core based on our biochemical analysis and determined the MHV fusion core structure. We also propose an important target site for fusion inhibitor design and several strategies, which have been successfully used in fusion inhibitor design for **human immunodeficiency virus** (**HIV**), for the treatment of SARS infection.

L23 ANSWER 22 OF 37 MEDLINE on STN

2004536660. PubMed ID: 15507629. Emergence of a drug-dependent **human immunodeficiency virus** type 1 variant during therapy with the T20 fusion inhibitor. Baldwin Chris E; Sanders Rogier W; Deng Yiqun; Jurriaans Suzanne; Lange Joep M; Lu Min; Berkhout Ben. (Department of Human Retrovirology, Academic Medical Center, University of Amsterdam, P.O. Box 22700, 1100 DE Amsterdam, The Netherlands.) Journal of virology, (2004 Nov) Vol. 78, No. 22, pp. 12428-37. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The fusion inhibitor T20 belongs to a new class of anti-**human immunodeficiency virus** type 1 (**HIV-1**) drugs designed to block entry of the virus into the host cell. However, the success of T20 has met with the inevitable emergence of drug-resistant **HIV-1** variants. We describe an evolutionary pathway taken by **HIV-1** to escape from the selective pressure of T20 in a treated patient. Besides the appearance of T20-resistant variants, we report for the first time the emergence of drug-dependent viruses with mutations in both the **HR1** and **HR2** domains of envelope glycoprotein 41. We propose a mechanistic model for the dependence of **HIV-1** entry on the T20 peptide. The T20-dependent mutant is more prone to undergo the conformational switch that results in the formation of the fusogenic six-helix bundle structure in gp41. A premature switch will generate nonfunctional envelope glycoproteins (dead spikes) on the surface of the virion, and T20 prevents this abortive event by acting as a safety pin that preserves an earlier prefusion

conformation.

L23 ANSWER 23 OF 37 MEDLINE on STN
2004428959. PubMed ID: 15334539. **HIV** fusion and its inhibition in antiretroviral therapy. Greenberg Michael; Cammack Nick; Salgo Miklos; Smiley Lynn. (Trimeris Inc., Durham, NC 27707, USA.. MGreenberg@trimeris.com) . Reviews in medical virology, (2004 Sep-Oct) Vol. 14, No. 5, pp. 321-37. Ref: 109. Journal code: 9112448. ISSN: 1052-9276. Pub. country: England: United Kingdom. Language: English.
AB The end of the twentieth century saw dramatic improvements in the prognosis of **HIV** infection brought about by the introduction of new agents (the protease inhibitors and the non-nucleoside reverse transcriptase inhibitors) and their use in highly active combinations. However, the durability of these combination treatments is limited by a number of factors including adverse effects and extensive intra-class cross-resistance so that new antiretrovirals acting on alternative targets and having improved systemic tolerability profiles are required. The **HIV** binding and entry process offers several potential targets for antiviral interaction. These include gp120 binding to CD4 and to chemokine co-receptor molecules as well as the fusion process itself, which involves interactions between two leucine zipper-like 4-3 repeat regions within gp41 known as heptad repeat (HR)1 and **HR2**. Peptides such as enfuvirtide (formerly DP178 or T-20), that mimic the **HR2** region of gp41, inhibit **HIV**-1 by a mechanism that is thought to involve competitive binding to **HR1**. This review summarises the clinical development of enfuvirtide, providing an overview of the pharmacokinetic, efficacy and safety data in various patient populations, and also considers the evidence for the key role of genotypic changes in the **HR1** region (amino acids 36-45) in determining viral susceptibility to inhibition by enfuvirtide.

L23 ANSWER 24 OF 37 MEDLINE on STN
2004343395. PubMed ID: 15123674. Structural basis for coronavirus-mediated membrane fusion. Crystal structure of mouse hepatitis virus spike protein fusion core. Xu Yanhui; Liu Yiwei; Lou Zhiyong; Qin Lan; Li Xu; Bai Zhihong; Pang Hai; Tien Po; Gao George F; Rao Zihe. (Laboratory of Structural Biology, Tsinghua University, Beijing 100084, China.) The Journal of biological chemistry, (2004 Jul 16) Vol. 279, No. 29, pp. 30514-22. Electronic Publication: 2004-04-27. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
AB The surface transmembrane glycoprotein is responsible for mediating virion attachment to cell and subsequent virus-cell membrane fusion. However, the molecular mechanisms for the viral entry of coronaviruses remain poorly understood. The crystal structure of the fusion core of mouse hepatitis virus S protein, which represents the first fusion core structure of any coronavirus, reveals a central hydrophobic coiled coil trimer surrounded by three helices in an oblique, antiparallel manner. This structure shares significant similarity with both the low pH-induced conformation of influenza hemagglutinin and fusion core of **HIV** gp41, indicating that the structure represents a fusion-active state formed after several conformational changes. Our results also indicate that the mechanisms for the viral fusion of coronaviruses are similar to those of influenza virus and **HIV**. The coiled coil structure has unique features, which are different from other viral fusion cores. Highly conserved heptad repeat 1 (**HR1**) and **HR2** regions in coronavirus spike proteins indicate a similar three-dimensional structure among these fusion cores and common mechanisms for the viral fusion. We have proposed the binding regions of **HR1** and **HR2** of other coronaviruses and a structure model of their fusion core based on our mouse hepatitis virus fusion core structure and sequence alignment. Drug discovery strategies aimed at inhibiting viral entry by blocking hairpin formation may be applied to the inhibition of a number of emerging infectious diseases, including severe acute

respiratory syndrome.

L23 ANSWER 25 OF 37 MEDLINE on STN
2004287732. PubMed ID: 15161975. Structural characterization of the fusion-active complex of severe acute respiratory syndrome (SARS) coronavirus. Ingallinella Paolo; Bianchi Elisabetta; Finotto Marco; Cantoni Giovanna; Eckert Debra M; Supekar Vinit M; Bruckmann Chiara; Carfi Andrea; Pessi Antonello. (Istituto di Ricerche di Biologia Molecolare P. Angeletti, Via Pontina Km 30.600, 00040 Pomezia, Italy.) Proceedings of the National Academy of Sciences of the United States of America, (2004 Jun 8) Vol. 101, No. 23, pp. 8709-14. Electronic Publication: 2004-05-25. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The causative agent of a recent outbreak of an atypical pneumonia, known as severe acute respiratory syndrome (SARS), has been identified as a coronavirus (CoV) not belonging to any of the previously identified groups. Fusion of coronaviruses with the host cell is mediated by the envelope spike protein. Two regions within the spike protein of SARS-CoV have been identified, showing a high degree of sequence conservation with the other CoV, which are characterized by the presence of heptad repeats (**HR1** and **HR2**). By using synthetic and recombinant peptides corresponding to the **HR1** and **HR2** regions, we were able to characterize the fusion-active complex formed by this novel CoV by CD, native PAGE, proteolysis protection analysis, and size-exclusion chromatography. **HR1** and **HR2** of SARS-CoV associate into an antiparallel six-helix bundle, with structural features typical of the other known class I fusion proteins. We have also mapped the specific boundaries of the region, within the longer **HR1** domain, making contact with the shorter **HR2** domain. Notably, the inner **HR1** coiled coil is a stable alpha-helical domain even in the absence of interaction with the **HR2** region. Inhibitors binding to HR regions of fusion proteins have been shown to be efficacious against many viruses, notably **HIV**. Our results may help in the design of anti-SARS therapeutics.

L23 ANSWER 26 OF 37 MEDLINE on STN
2004285974. PubMed ID: 15186521. Sensitivity of **HIV** type 1 subtype C isolates to the entry inhibitor T-20. Cilliers Tonie; Patience Trudy; Pillay Candice; Papathanasopoulos Maria; Morris Lynn. (AIDS Virus Research Unit, National Institute for Communicable Diseases, Johannesburg, South Africa.) AIDS research and human retroviruses, (2004 May) Vol. 20, No. 5, pp. 477-82. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB T-20 is the first in a new class of antiretroviral drugs targeting the entry stage of the virus life cycle. It is a 36 amino acid peptide that binds to the **HR1** region of gp41 preventing gp41-mediated fusion with the host cell membrane. T-20 was designed based on the **HR2** sequence of **HIV**-1 subtype B gp41, a region that shows significant genetic variation with **HIV**-1 subtype C sequences. In order to assess the efficacy of T-20 to inhibit subtype C isolates, a total of 23 isolates were tested for their ability to replicate in the presence of T-20. This included 15 isolates that used CCR5, five that used both CCR5 and CXCR4, and three that used CXCR4. Five of these were from patients failing other antiretroviral therapies. Sequence analysis of the **HR2** region indicated that there were 10-16 amino acid changes in the region corresponding to T-20. However, all isolates were effectively inhibited by T-20 at 1 microg/ml. There were no significant differences between viruses that used CCR5 or CXCR4 to enter cells. All isolates, except one, had GIV at positions 36-38 in the **HR1** region. One isolate had a GVV motif but this did not affect its sensitivity to T-20. Therefore, T-20 inhibited subtype C viruses despite significant genetic differences in the **HR2** region and there was no evidence for baseline resistance to T-20. These data suggest that T-20 would be highly effective in patients with **HIV**-1 subtype C

infection, including those failing existing antiretroviral drug regimens.

L23 ANSWER 27 OF 37 MEDLINE on STN
2004282635. PubMed ID: 15184046. Suppression of SARS-CoV entry by peptides corresponding to heptad regions on spike glycoprotein. Yuan Kehu; Yi Ling; Chen Jian; Qu Xiuxia; Qing Tingting; Rao Xi; Jiang Pengfei; Hu Jianhe; Xiong Zikai; Nie Yuchun; Shi Xuanling; Wang Wei; Ling Chen; Yin Xiaolei; Fan Keqiang; Lai Luhua; Ding Mingxiao; Deng Hongkui. (Department of Cell Biology and Genetics, College of Life Sciences, Peking University, Beijing 100871, PR China.) Biochemical and biophysical research communications, (2004 Jul 2) Vol. 319, No. 3, pp. 746-52. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.
AB Heptad repeat regions (**HR1** and **HR2**) are highly conserved sequences located in the glycoproteins of enveloped viruses. They form a six-helix bundle structure and are important in the process of virus fusion. Peptides derived from the HR regions of some viruses have been shown to inhibit the entry of these viruses. SARS-CoV was also predicted to have **HR1** and **HR2** regions in the S2 protein. Based on this prediction, we designed 25 peptides and screened them using a **HIV**-luc/SARS pseudotyped virus assay. Two peptides, **HR1**-1 and **HR2**-18, were identified as potential inhibitors, with EC(50) values of 0.14 and 1.19microM, respectively. The inhibitory effects of these peptides were validated by the wild-type SARS-CoV assay. **HR1**-1 and **HR2**-18 can serve as functional probes for dissecting the fusion mechanism of SARS-CoV and also provide the potential of further identifying potent inhibitors for SARS-CoV entry.

L23 ANSWER 28 OF 37 MEDLINE on STN
2004235473. PubMed ID: 15113923. CD4-induced T-20 binding to **human immunodeficiency virus** type 1 gp120 blocks interaction with the CXCR4 coreceptor. Yuan Wen; Craig Stewart; Si Zhihai; Farzan Michael; Sodroski Joseph. (Department of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115, USA.) Journal of virology, (2004 May) Vol. 78, No. 10, pp. 5448-57. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.
AB The synthetic peptide T-20, which corresponds to a sequence within the C-terminal heptad repeat region (**HR2**) of the **human immunodeficiency virus** type 1 (**HIV**-1) gp41 envelope glycoprotein, potently inhibits viral membrane fusion and entry. Although T-20 is thought to bind the N-terminal heptad repeat region (**HR1**) of gp41 and interfere with gp41 conformational changes required for membrane fusion, coreceptor specificity determined by the V3 loop of gp120 strongly influences the sensitivity of **HIV**-1 variants to T-20. Here, we show that T-20 binds to the gp120 glycoproteins of **HIV**-1 isolates that utilize CXCR4 as a coreceptor in a manner determined by the sequences of the gp120 V3 loop. T-20 binding to gp120 was enhanced in the presence of soluble CD4. Analysis of T-20 binding to gp120 mutants with variable loop deletions and the reciprocal competition of T-20 and particular anti-gp120 antibodies suggested that T-20 interacts with a gp120 region near the base of the V3 loop. Consistent with the involvement of this region in coreceptor binding, T-20 was able to block the interaction of gp120-CD4 complexes with the CXCR4 coreceptor. These results help to explain the increased sensitivity of CXCR4-specific **HIV**-1 isolates to the T-20 peptide. Interactions between the gp41 **HR2** region and coreceptor-binding regions of gp120 may also play a role in the function of the **HIV**-1 envelope glycoproteins.

L23 ANSWER 29 OF 37 MEDLINE on STN
2004175337. PubMed ID: 15051887. Small-molecule inhibitors of **HIV**-1 entry block receptor-induced conformational changes in the viral envelope glycoproteins. Si Zhihai; Madani Navid; Cox Jason M; Chruma Jason J; Klein Jeffrey C; Schon Arne; Phan Ngoc; Wang Liping; Biorn Alyssa C; Cocklin

Simon; Chaiken Irwin; Freire Ernesto; Smith Amos B 3rd; Sodroski Joseph G. (Department of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, Boston, MA 02115, USA.) Proceedings of the National Academy of Sciences of the United States of America, (2004 Apr 6) Vol. 101, No. 14, pp. 5036-41. Electronic Publication: 2004-03-29. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB When interacting with the CD4 receptor, the **HIV** gp120 envelope glycoprotein undergoes conformational changes that allow binding to the chemokine receptor. Receptor binding is proposed to lead to conformational changes in the gp41 transmembrane envelope glycoprotein involving the creation and/or exposure of a coiled coil consisting of three heptad repeat (HR) sequences. The subsequent interaction of the **HR2** region of gp41 with this coiled coil results in the assembly of a six-helix bundle that promotes the fusion of the viral and target cell membranes. Here we show that CD4 binding to gp120 induces the formation and/or exposure of the gp41 **HR1** coiled coil in a process that does not involve gp120 shedding and that depends on the proteolytic maturation of the gp160 envelope glycoprotein precursor. Importantly, BMS-806 and related **HIV**-1 entry inhibitors bind gp120 and block the CD4 induction of **HR1** exposure without significantly affecting CD4 binding. Moreover, these compounds do not disrupt gp120-chemokine receptor binding or the **HR1**-**HR2** interaction within gp41. These studies thus define a receptor-induced conformational rearrangement of gp120-gp41 that is important for both CD4-dependent and CD4-independent **HIV**-1 entry and is susceptible to inhibition by low-molecular-weight compounds.

L23 ANSWER 30 OF 37 MEDLINE on STN

2004151843. PubMed ID: 15043961. Interaction between heptad repeat 1 and 2 regions in spike protein of SARS-associated coronavirus: implications for virus fusogenic mechanism and identification of fusion inhibitors. Liu Shuwen; Xiao Gengfu; Chen Yibang; He Yuxian; Niu Jinkui; Escalante Carlos R; Xiong Huabao; Farmar James; Debnath Asim K; Tien Po; Jiang Shibo. (Lindsley F Kimball Research Institute, New York Blood Center, New York, NY 10021, USA.) Lancet, (2004 Mar 20) Vol. 363, No. 9413, pp. 938-47. Journal code: 2985213R. E-ISSN: 1474-547X. Pub. country: England: United Kingdom. Language: English.

AB BACKGROUND: Studies on the fusion-inhibitory peptides derived from the heptad repeat 1 and 2 (**HR1** and **HR2**) regions of the **HIV**-1 envelope glycoprotein gp41 provided crucial information on the viral fusogenic mechanism. We used a similar approach to study the fusogenic mechanism of severe-acute-respiratory-syndrome-associated coronavirus (SARS-CoV). METHODS: We tested the inhibitory activity against infection of two sets of peptides corresponding to sequences of SARS-CoV spike protein **HR1** and **HR2** regions and investigated the interactions between the **HR1** and **HR2** peptides by surface plasmon resonance, sedimentation equilibration analysis, circular dichroism, native polyacrylamide-gel electrophoresis, size exclusion high-performance liquid chromatography, and computer-aided homology modelling and molecule docking analysis. FINDINGS: One peptide, CP-1, derived from the **HR2** region, inhibited SARS-CoV infection in the micromolar range. CP-1 bound with high affinity to a peptide from the **HR1** region, NP-1. CP-1 alone had low alpha-helicity and self-associated to form a trimer in phosphate buffer (pH 7.2). CP-1 and NP-1 mixed in equimolar concentrations formed a six-helix bundle, similar to the fusogenic core structure of **HIV**-1 gp41. INTERPRETATION: After binding to the target cell, the transmembrane spike protein might change conformation by association between the **HR1** and **HR2** regions to form an oligomeric structure, leading to fusion between the viral and target-cell membranes. At the prefusion intermediate state, CP-1 could bind to the **HR1** region and interfere with the conformational changes, resulting in inhibition of SARS-CoV fusion with the target cells. CP-1 might be modifiable to increase its anti-SARS-CoV activity and could be further developed as an antiviral agent for treatment or prophylaxis of SARS-CoV

infection.

L23 ANSWER 31 OF 37 MEDLINE on STN

2004107891. PubMed ID: 14998221. Enfuvirtide; a new fusion inhibitor for therapy of **human immunodeficiency virus** infection. Hardy Helene; Skolnik Paul R. (Center for HIV/AIDS Care and Research, Boston Medical Center, Massachusetts 02118, USA.. helene.hardy@bmc.org) . Pharmacotherapy, (2004 Feb) Vol. 24, No. 2, pp. 198-211. Journal code: 8111305. ISSN: 0277-0008. Pub. country: United States. Language: English.

AB Enfuvirtide is the first fusion inhibitor to be approved by the Food and Drug Administration for the treatment of chronic **human immunodeficiency virus** (**HIV**) infection in adults and children 6 years and older. The drug is a synthetic peptide derived from a naturally occurring amino acid sequence known as heptad repeat 2 (**HR2**) found in gp41, a viral transmembrane glycoprotein that facilitates fusion with host cells. By mimicking the activity of **HR2** and competitively binding to a second region of gp41, heptad repeat 1 (**HR1**), enfuvirtide prevents interaction between **HR1** and **HR2** and inhibits the conformational change of gp41 that is necessary for fusion of virions to host cells. The safety and efficacy of enfuvirtide have been studied only in antiretroviral-experienced persons. Preliminary data from two multicenter phase III clinical trials (T-20 versus Optimized Regimen Only [TORO 1, TORO 2]) suggest that the drug is safe and efficacious in heavily pretreated subjects through 24 weeks. By week 24, in TORO 1 and TORO 2, respectively, mean changes in **HIV** RNA concentrations of -1.7 and -1.4 log10 copies/ml were observed in subjects receiving enfuvirtide plus an optimized background (OB) regimen, compared with changes of -0.8 and -0.7 log10 copies/ml in subjects receiving an OB regimen alone. Resistance to enfuvirtide has been identified in vitro and in vivo. Most resistant variants contain mutations in the **HR1** region of gp41 (positions 36-45). In phase III clinical trials, numerous substitutions within this critical region were associated with faster time to virologic failure over 24 weeks. Overall, enfuvirtide appears to be well tolerated and acceptable to patients despite a high rate of injection site reactions (> 90%). Bacterial pneumonia and eosinophilia occurred more frequently in subjects taking enfuvirtide than in those taking an OB regimen alone in phase III trials; however, no causal relationship was established. Like most drugs with peptide structures, enfuvirtide appears to have a low potential for metabolic drug-drug interactions. The approved dosage is 90 mg twice/day by subcutaneous injection in adults and 2 mg/kg twice/day in children older than 6 years. Enfuvirtide is an addition to antiretroviral therapy since it targets a new step in the **HIV** life cycle. Given the complexity of its production and administration, however, it is likely to be most useful in antiretroviral-experienced patients.

L23 ANSWER 32 OF 37 MEDLINE on STN

2003565061. PubMed ID: 14651977. Mutations in gp41 and gp120 of **HIV**-1 isolates resistant to hexa-arginine neomycin B conjugate. Borkow Gadi; Lara Humberto Herman; Lapidot Aviva. (Department of Organic Chemistry, The Weizmann Institute of Science, 76100, Rehovot, Israel.) Biochemical and biophysical research communications, (2003 Dec 26) Vol. 312, No. 4, pp. 1047-52. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Aminoglycoside-arginine conjugates (AACs) inhibit **HIV**-1 replication and act as Tat antagonists. AACs compete with monoclonal antibody binding to CXCR4, compete with SDF-1alpha and **HIV**-1 gp120 cellular uptake, indicating that they interfere with initial steps of **HIV**-1 infection. We here present the selection of **HIV**-1 isolates resistant to hexa-arginine neomycin B conjugate (NeoR6), the most potent anti-**HIV**-1 AAC. We found in the NeoR6-resistant isolates the following mutations in gp120: I339T in the C3 region, S372L in the V4 region, and Q395K in the C4 region; and in gp41: S668R and F672Y in the 'heptad repeat' 2 (**HR2**)

region. These findings strongly suggest that NeoR6 obstructs **HIV**-1 replication by interfering with the fusion step, dependent on both conformational changes in gp120 following CD4 and CXCR4 interaction, as well as by conformational changes in gp41 induced by **HR1** and **HR2** interaction. The AACs may thus represent a novel family of fusion inhibitors.

L23 ANSWER 33 OF 37 MEDLINE on STN

2003152836. PubMed ID: 12615056. Both heptad repeats of human respiratory syncytial virus fusion protein are potent inhibitors of viral fusion. Wang Enxiu; Sun Xiao'ou; Qian Yuan; Zhao Linqing; Tien Po; Gao George F. (Department of Molecular Virology and Bio-Engineering, Institute of Microbiology, Chinese Academy of Sciences, Zhongguancun Beiyitiao, Beijing 100080, China.) Biochemical and biophysical research communications, (2003 Mar 14) Vol. 302, No. 3, pp. 469-75. Journal code: 0372516. ISSN: 0006-291X. Pub. country: United States. Language: English.

AB Heptad repeat regions (**HR1** and **HR2**) are highly conserved peptides located in F(1) of paramyxovirus envelope proteins. They are important in the process of virus fusion and form six-helix bundle structure (trimer of **HR1** and **HR2** heterodimer) post-fusion, similar to those found in the fusion proteins of other enveloped viruses, such as retrovirus **HIV**. Both **HR1** and **HR2** show potent inhibition for virus fusion in some members of paramyxovirus. However, in other members, only **HR2** gives strong inhibition whereas **HR1** does not. Human respiratory syncytial virus (hRSV) is a member of paramyxovirus and its crystal structure of **HR1** and **HR2** six-helix bundle was solved lately. Although hRSV **HR2** inhibition was reported, nevertheless the effect of **HR1** on virus fusion is not known. In this study, hRSV **HR1** and **HR2** were expressed as fusion protein separately in Escherichia coli system and their complex assembly and virus fusion inhibition effect have been analysed. It shows that both **HR1** and **HR2** (in the fusion form with 50-amino-acid fusion partner) of hRSV F protein give strong inhibition on virus fusion (IC(50) values are 1.68 and 2.93 microM, respectively) and they form stable six-helix bundle in vitro with both in the fusion protein form.

L23 ANSWER 34 OF 37 MEDLINE on STN

2002430478. PubMed ID: 12186891. C-Terminal gp40 peptide analogs inhibit feline immunodeficiency virus: cell fusion and virus spread. Medinas R J; Lambert D M; Tompkins W A. (Immunology Program, North Carolina State University, Raleigh 27606, USA.) Journal of virology, (2002 Sep) Vol. 76, No. 18, pp. 9079-86. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The envelope glycoprotein of **human immunodeficiency virus** type 1 (**HIV**-1), gp160, is synthesized as a protein precursor that when proteolytically cleaved yields two subunits, gp120 and gp41. gp120 is the surface glycoprotein on **HIV**-1 responsible for binding to CD4, and gp41 is the transmembrane glycoprotein involved in the membrane fusion process. gp41 is divided into the N-terminal fusion peptide, the heptad repeat 1 (**HR1**) and **HR2** regions, and the C-terminal transmembrane region, which are collectively responsible for virus fusion and entry into the cell. Synthetic peptides derived from the **HR2** and **HR1** regions of **HIV**-1(LAI) have been shown to prevent virus-cell fusion and infection in vitro. In phase II clinical trials in **HIV** patients, data revealed that T20 has antiviral efficacy and is well tolerated. Similar results were obtained in vitro with **HIV**-2 and simian immunodeficiency virus, supporting the conservation of the gp41 ectodomain among lentiviruses. Feline immunodeficiency virus (FIV) infection in the cat has been used as a model to develop potential antivirals for **HIV**. To determine if synthetic gp40 analogs capable of inhibiting FIV infection could be identified, 15 overlapping 35-amino-acid peptides derived from the C-terminal **HR2** domain of FIV gp40 were synthesized. These peptides were tested for efficacy against FIV in a syncytium-forming assay with

FIV-infected CrFK cells and HeLa cells expressing the FIV receptor CXCR4. Several peptides exhibited activity at the nanogram level. Antiviral activity was confirmed by suppression of reverse transcriptase in a FIV feline CD4(+)-T-cell (FCD4-E) acute-infection assay. These data demonstrate that synthetic peptides derived from the **HR2** domain of the FIV gp41 protein are effective inhibitors of FIV infection.

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2002417436. PubMed ID: 12172081. Variability of critical epitopes within **HIV**-1 heptad repeat domains for selected entry inhibitors in **HIV**-infected populations worldwide [corrected]. Hanna Sheri L; Yang Chunfu; Owen Sherry M; Lal Renu B. (HIV Immunology and Diagnostics Branch, Division of AIDS, STD, and TB Laboratory Research, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.) AIDS (London, England), (2002 Aug 16) Vol. 16, No. 12, pp. 1603-8. Journal code: 8710219. ISSN: 0269-9370. Pub. country: England: United Kingdom. Language: English.

AB BACKGROUND: Two of the fusion inhibitors T-20 and 5-helix polypeptide have been shown to be potent inhibitors of cell-to-cell fusion and are currently under investigation as therapy for **HIV**-1. OBJECTIVES: To examine variability of **HIV**-1 gp41 heptads repeat regions (**HR1** and **HR2**), with special emphasis on the presence of T-20 resistance mutations and 5-helix variability at critical epitopes, in treatment-naive patients infected with diverse **HIV**-1 subtypes from different geographic regions. METHODS: A total of 150 specimens representing **HIV**-1 group M subtypes (A-G) from persons naive to **HIV**-1 viral entry inhibitor therapy were used to amplify and sequence a 506 bp segment of transmembrane protein. RESULTS: In general, both **HR1** (a.a. 540-593) and **HR2** (a.a. 628-673) domains were highly conserved. Sequence analysis of the T-20 resistant domain (a.a. 547-549, GIV) revealed that 99% of the specimens (149 of 150) carried a T-20 sensitive genotype. The critical epitopes involved in the 5-helix interaction include residues at positions 628W, 631W, 635I, 638Y, 642I, 645L, 649S, 652Q, 656N, and 659E. Analysis of the 150 specimens revealed that all had identical residues at six of these positions, whereas two positions had minor variations (635 and 649) and two (645 and 659) appeared to have subtype-specific substitutions. CONCLUSIONS: This data indicates that there is limited resistance to T-20 in these worldwide populations and that the critical epitopes for effective 5-helix binding are highly conserved across all subtypes. Taken together, these data suggest that T-20 and 5-helix should provide useful additives to current antiretroviral therapy for clinical management of **HIV** disease.

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2001462471. PubMed ID: 11507206. Sensitivity of **human immunodeficiency virus** type 1 to fusion inhibitors targeted to the gp41 first heptad repeat involves distinct regions of gp41 and is consistently modulated by gp120 interactions with the coreceptor. Derdeyn C A; Decker J M; Sfakianos J N; Zhang Z; O'Brien W A; Ratner L; Shaw G M; Hunter E. (Department of Microbiology, Birmingham, Alabama 35294, USA.) Journal of virology, (2001 Sep) Vol. 75, No. 18, pp. 8605-14. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB T-20 is a synthetic peptide that corresponds to 36 amino acids within the C-terminal heptad repeat region (**HR2**) of **human immunodeficiency virus** type 1 (**HIV**-1) gp41. T-20 has been shown to potently inhibit viral replication of **HIV**-1 both in vitro and in vivo and is currently being evaluated in a Phase III clinical trial. T-649 is an inhibitory peptide that also corresponds to 36 amino acids within **HR2**. This sequence overlaps the T-20 sequence but is shifted 10 residues toward the N terminus of gp41. Both inhibitors are thought to exert their antiviral activity by interfering with the conformational changes that occur within gp41 to promote membrane fusion following gp120 interactions with CD4 and coreceptor molecules. We have shown previously that coreceptor

specificity defined by the V3 loop of gp120 modulates sensitivity to T-20 and that a critical region within the N-terminal heptad repeat (**HR1**) of gp41 is the major determinant of sensitivity (C. A. Derdeyn et al., J. Virol. 74:8358-8367, 2000). This report shows that (i) regions within gp41 distinct from those associated with T-20 sensitivity govern the baseline sensitivity to T-649 and (ii) T-649 sensitivity of chimeric viruses that contain sequences derived from CXCR4- and CCR5-specific envelopes is also modulated by coreceptor specificity. Moreover, the pattern of sensitivity of CCR5-specific chimeras with only minor differences in their V3 loop was consistent for both inhibitors, suggesting that the individual affinity for coreceptor may influence accessibility of these inhibitors to their target sequence. Finally, an analysis of the sensitivity of 55 primary, inhibitor-naive **HIV**-1 isolates found that higher concentrations of T-20 ($P < 0.001$) and T-649 ($P = 0.016$) were required to inhibit CCR5-specific viruses compared to viruses that utilize CXCR4. The results presented here implicate gp120-coreceptor interactions in driving the complex conformational changes that occur in gp41 to promote fusion and entry and suggest that sensitivity to different **HR1**-directed fusion inhibitors is governed by distinct regions of gp41 but is consistently modulated by coreceptor specificity.

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2001201555. PubMed ID: 11153086. Monoclonal antibodies that bind to the core of fusion-active glycoprotein 41. Chen C H; Greenberg M L; Bolognesi D P; Matthews T J. (Department of Microbiology, Meharry Medical College, Nashville, Tennessee 37208, USA.. cchen@mail.mmc.edu) . AIDS research and human retroviruses, (2000 Dec 10) Vol. 16, No. 18, pp. 2037-41. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB The heptad repeat regions **HR1** and **HR2** of **HIV**-1 gp41 can associate to form heterooligomers through helical coil-coil interactions that are believed to play a key role in virus-induced membrane fusion. The **HR1**/**HR2** complex was proposed to be the core structure of the fusion-active conformation of gp41. Here, we show that two human monoclonal antibodies, Fab-d and 50-69, specifically recognize the putative fusion-active conformation of gp41. Fab-d binding requires the interaction between the **HR1** and **HR2** regions of gp41. The reactivity of human monoclonal antibody 50-69 to the C terminus of the **HR1** sequence is dependent on the helical structure of **HR1**. It appears that **HR2** is able to interact with **HR1** and, subsequently, induce an epitope in **HR1** that is required for 50-69 binding. Mutations that disrupt the helical structure of **HR1** significantly compromise Fab-d and 50-69 binding. Although the epitopes are not identical, the ability of Fab-d to partially compete with 50-69 binding suggests a close proximity of the two epitopes. Antibodies that are able to interact with the core of the putative fusion-active gp41 may be useful in further unveiling the mechanism of **HIV**-induced membrane fusion.

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